IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#28
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L. Tyson
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In Re Application Of

LOUIS D. FALO, JR. ET AL.

Serial No. 08/931,219

Filed September 19, 1997

Entitled

STIMULATION OF CELL-MEDIATED IMMUNE RESPONSES BY TARGETED PARTICULATE GENETIC IMMUNIZATION

File Wrapper Continuation of Application No. 08/535,566, filed September 28, 1995, and now abandoned.

Group Art Unit 1632

Examiner Jill D. Martin

Attorney Docket No. 125350-3

APPEAL BRIEF

February 10, 2000

Assistant Commissioner for Patents
BOX AF
Washington, D.C. 20231

Sir:

Appellants respectfully appeal the final rejection issued in the above-captioned case on June 9, 1999, and maintained in the Advisory Action issued on January 24, 2000.

Real Party In Interest

The real parties in interest are the University of Pittsburgh of the Commonwealth System of Higher Education and the Dana-Farber Cancer Institute, Inc. Assignments transferring all of the inventors' rights, title and interest to the University and Dana-Farber were executed by the inventors from each institution on June 18, 1997 and June 3, 1997, respectively, and were recorded in the United States Patent and Trademark Office on June 27, 1997 at Reel 8578, Frame 0769, and at Reel 8578, Frame 0772, respectively.

Related Appeals and Interferences

There are no related appeals or interferences that would be believed to directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

Status of Claims

Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 are pending and appealed. The appealed claims are listed in the attached appendix. Claims 4, 18, 33, 48 and 62 have been cancelled.

Status of the Amendments

The pending claims were finally rejected in an Office Action mailed June 9, 1999. Appellants filed a Response and Amendment to this Office Action on December 8, 1999. The Advisory Action mailed January 24, 2000 indicates the Amendment has not been entered.

Summary of the Invention

The present invention is directed to *in vivo* methodologies of treating a mammalian host capable of generating an immune response, by generating a DNA fragment that expresses an antigenic protein or fragment thereof, distributing the DNA fragment on a particle surface to create a particulate polynucleotide, and inoculating the host with the particulate polynucleotide; the particulate polynucleotide is delivered to the cytoplasm of an antigen presenting cell ("APC") within the host. The expressed antigenic protein or fragment thereof is presented to the membrane surface of an APC through the MHC Class I pathway; this presentation elicits an immune response in the host resulting in the destruction of neoplastic or virally infected cells. Inoculation can be by any means known in the art including through use of a biolistic device (Claims 15-16, 17-28) or by direct inoculation (Claims 29-32, 34-43). *Ex vivo* methods are also included in the present invention, wherein the particulate polynucleotide is delivered to the cytoplasm of an APC *in vitro*, and the mammalian host is inoculated with the APC by direct injection (Claims 44-47, 49-58). In one embodiment of the *ex vivo* methodology, the DNA expresses a molecule that enhances the antigen presenting function of an APC (Claims 59-61, 63-67). The present invention is also directed to methods for transfecting APCs by delivering to the cytoplasm of the APC a particulate polynucleotide coated with a DNA fragment that expresses an antigenic protein or fragment thereof (Claims 68-70). A method of inducing a CTL immune response by transfecting APCs, *in vivo*, with a DNA fragment which expresses an antigenic protein or fragment thereof, such that said protein is presented to the membrane surface of the APC through the MHC Class I pathway and tumor cells are destroyed is recited in Claim 71.

Issues

The issues presented on appeal are as follows:

1. Whether Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 are unpatentable over 35 U.S.C. § 112, first paragraph, for lack of enablement;

2. Whether Claims 1-3, 5-17, 19-32, 34-47 and 49-61 are unpatentable under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter of the invention;

3. Whether Claims 1, 15, 29 and 68-71 are unpatentable under 35 U.S.C. § 102(b) as being anticipated by either Tang et al. or Barry et al.;

4. Whether Claims 1, 15, 29 and 68-71 are unpatentable under 35 U.S.C. § 102(b) as being anticipated by Hui et al.;

5. Whether 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 are unpatentable under 35 U.S.C. § 103(a) as being unpatentable over Weiner et al. taken with either Tang or Barry.

Grouping of Claims

Claims 1-3, and 4-14 stand or fall together; Claims 15-17 and 19-28 stand or fall together as they are directed to a particular mode of delivery which can be patentable over other modes; Claims 29-32 and 34-43 stand or fall together as they are directed to a particular mode of delivery which can be patentable over other modes; Claims 44-47 and 49-58 stand or fall together as they are directed to an *ex vivo* methodology which can be patentable over *in vivo* methods; Claims 59-61 and 63-67 stand or fall together as they are directed to an *ex vivo* methodology using a particular type of molecule, which can be patentable over *in vivo* methodologies or other *ex vivo* methodologies; Claims 68-70 stand or fall together as being drawn to methods for transfecting APCs, which can be patentable over the other claimed methods; and Claim 71 stands or falls alone as being directed to a method of inducing a CTL immune response, which can be patentable over the other claimed methods.

Argument

The claims of the present invention generally relate to methods of eliciting an immune response in a host through the use of particulate polynucleotides coated with DNA fragments that express antigenic proteins or fragments thereof. By delivering these particulate polynucleotides to the cytoplasm of antigen presenting cells ("APCs"), antigenic proteins or fragments thereof are presented to the membrane of the APCs through the MHC Class I pathway. As will be appreciated by those skilled in the art, such presentation stimulates the induction of antigen-specific cytotoxic T lymphocytes ("CTLs"). Induced antigen-specific CTLs then target and destroy antigenic expressing host cells, such as neoplastic cells or virally infected cells. The antigen-specific immune response depends on the particle antigen expressed by the

DNA sequence coated on the particulate polynucleotide. The present invention can be carried out by either *ex vivo* or *in vivo* methods. A specific embodiment of the *ex vivo* methods is one in which the antigenic protein or fragment thereof is a molecule which enhances the antigen presentation function of an APC. The invention is also generally directed to methods for transfecting APCs, and a method for eliciting a CTL immune response through transfection of APCs.

Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 were rejected as allegedly lacking enablement. One skilled in the art, however, would clearly be able to practice the invention of the pending claims based upon the teachings of the specification as filed. The Examiner concedes in the June 9, 1999 Office Action ("last Office Action") that Appellants' evidence clearly demonstrates that particle bombardment administration into skin results in CTL mediated immune responses to tumors or viruses, and then concludes that Appellants' claims should be limited to 1) particle bombardment, 2) administration into skin, and 3) eliciting a CTL immune response. According to the Examiner, Appellants' "specification fails to teach or provide guidance to the skilled artisan for preparing vectors for APC cell-targeting by any other route of administration . . . ." Appellants submit that it is improper to limit the invention in the manner suggested by the Examiner.

More specifically, both biolistic gene gun methods and direct injection methods of administration are taught and enabled by the specification. Example sections 7 and 8 (and corresponding figures) clearly show that biolistic immunization is an effective means for accomplishing the present methods, and that subcutaneous injection of particulate polynucleotides is as effective as the biolistic approach in eliciting an immune response. Appellants respectfully submit that this supports claims generically encompassed by these and other methods; in addition, the claims directed to specific means for immunization (*i.e.*, biolistic and direct injection) are clearly enabled. In light of this evidence, there would not appear to be any need to "provide guidance to the skilled artisan for preparing vectors for APC cell targeting . . ." as suggested by the Examiner. Appellants have repeatedly pointed to their example evidence regarding direct injection. Nonetheless, the Examiner continues to maintain the position that there is no guidance for practicing the invention by any route of administration other than the biolistic approach. This clearly ignores the example evidence that confirms the efficacy of other methods, namely direct injection.

Because the examples provide evidence that direct injection is an effective means of immunization according to the present invention, the examples also provide evidence that injection to points other than the skin are effective. This is discussed in, for example, example section 7, page 25, lines 25-29, in which subcutaneous injection is discussed. Accordingly, the Examiner's statement that no evidence is supplied regarding administration to points other than the skin is also erroneous.

Appellants further submit that Claim 1-3, 5-17, 19-32, 34-37 and 49-61 are not indefinite. The Examiner previously rejected these claims under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable methods of treating hosts afflicted with a naturally occurring disease that may evade immune system recognition. In response, Appellants amended Claims 1, 15, 29, 44 and 59 to recite that the present invention is directed to mammalian hosts that are "capable of generating an immune response." It is well known and established in the art that patients with, for example, late stage tumors, viral infections, or the like, can demonstrate general immunosuppression. The presence or absence of such generalized immunosuppresion, and the general immune status of patients, is routinely determined as a part of the medical care of these patients. Clearly, a patient generally incapable of mounting an immune response would not be a candidate for the immunotherapeutic methods taught in the present invention; significantly, such a patient would most likely not be a candidate for *any* form of immunotherapy. As the general immune status of candidates for immunotherapy, or any other form of anti-cancer or anti-viral therapy, is routinely determined, such a determination relevant to the applicability of the methods of the present invention cannot be considered undue experimentation.

In response to the amendment the Examiner rejected the claims under 35 U.S.C. § 112, second paragraph, stating that the term "capable of eliciting an immune response" renders the claims indefinite "because the capacity of a subject to perform some function is merely a latent characteristic of said subject and said language carries no patentable weight." The Examiner suggested instead "that Applicant use claim language which clearly indicates that the mammalian host is fully immunocompetent, *i.e.*, has a fully functional immune system intact." The Examiner's suggestion, however, ignores the fact that Appellants' invention is directed to any mammalian host capable of mounting an immune response, including those who are less than fully immunocompetent. Indeed, limiting the invention to those who are fully immunocompetent would prevent this invention's therapeutic use on numerous patients, such as cancer patients, who are less than fully immunocompetent yet are still capable of mounting some immune response. In addition, the phrase "capable of generating an immune response" describes the mammalian host to whom the present methods are directed; hosts incapable of generating an immune response would not be appropriately treated by the present methods, or any other methods for that matter. Thus, the added language does more than identify a "latent characteristic" of the host. Even if that was all it did, which Appellants do not concede, Appellants fail to see how using the "fully immunocompetent" language suggested by the Examiner is any less descriptive of a latent characteristic than the phrase "capable of generating an immune response".

Appellants submit that one of ordinary skill in the art would understand what is presently claimed, in light of the specification and the general level of knowledge in the art. As noted above, those skilled in the art know that only patients capable of mounting some sort of immune response are appropriate candidates for any form of immunotherapy. In addition, the language "capable of generating an immune response" has been allowed in the claims of U.S. Patent No. 5,951,975 submitted with Appellants December 18, 1999 response and attached hereto at Tab A. Appellants submit this patent as evidence that the added language is understandable to those skilled in the art. For all of these reasons, Appellants submit that the Claims 1-3, 5-17, 19-32, 34-47 and 49-61 are not indefinite.

Claims 1, 15, 29 and 68-71 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by either Tang et al. (*Nature* 1992) or Barry et al. (*Biotechniques* 1994). Neither Tang nor Barry, however, teach all of the elements of the present invention.

More specifically, the present claims recite elicitation of an immune response, particularly an anti-tumor or anti-viral immune response that destroys neoplastic or virally infected cells; this response is through the MHC Class I pathway, as specifically recited in the claims. As noted previously, those skilled in the art will recognize that presentation via the MHC Class I pathway results in elicitation of a CTL response. In any event, the specification as filed makes clear that the present invention is directed to such a response. (See, for example, page 1, lines 25-28; page 2, lines 1-8). It would be apparent to one skilled in the art, therefore, based upon a review of the claims in conjunction with the specification, that Appellants are claiming a different response than that taught by either Tang or Barry. Both Tang and Barry teach an antibody response. The mechanism by which an antibody response is triggered is different from that by which a CTL response is elicited. Antibody responses are not related to Class I presentation; antibody responses require Class II presentation to helper T cells, not to CTLs. Antibody responses further require that the presented protein be recognized by B cells. Thus, the APC must have an external source of antigenic protein. In the present invention, the source of antigen is internal to the APC, *i.e.*, produced by the APC receiving the delivered DNA. Thus, targeting delivery of DNA to the cytoplasm of APCs according to the present invention targets Class I presentation of the antigen, which induces a CTL response. This is not taught in either of the cited references. Moreover, antibody responses are not generally effective against tumor cells or virally infected cells as are Appellants' claimed methods. Thus, the methods of Tang and Barry teach a different route of action and a different result as compared to the present methods.

The Examiner states that "Antigen processing and presentation via MHC Class I can initiate a variety of immune reactions which would also encompass the generation of antibodies." Neither the Tang nor Barry articles support this

proposition, however. There is no mention in either article of eliciting an antibody response through the MHC Class I pathway. For all of these reasons, Appellants submit that all of the claims rejected on this basis are allowable.

In addition, both Tang et al. and Barry et al. teach the use of a gene gun or biolistic device. Claim 29, however, is specifically directed to use of direct injection, and not a biolistic device. Thus, neither of the references teach the specific method of Claim 29; that claim is therefore further allowable over the art. Neither reference teaches transfection of APCs as recited in Appellants Claims 68-70, especially the *in vivo* methodology of Claim 70. These claims are therefore further allowable over the art. Finally, Claim 71 is specifically directed to a method of inducing a CTL immune response through the MHC Class I pathway so as to destroy tumor cells. Neither Tang nor Barry teach elicitation of a CTL response. Accordingly, Claim 71 is therefore further allowable over the cited art.

To establish anticipation under 35 U.S.C. § 102, every element of a claim must be present in a single reference. (See, for example, *Jamesbury Corporation v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985), a copy of which is attached at Tab B.) Not every element of Claims 1, 15, 29 and 68-71 is taught by the two references. Specifically, the references do not teach delivery of an antigenic protein or fragment thereof to professional APCs, such that said protein or fragment thereof is presented through the MHC Class I restricted pathway by the APC. In addition, neither of the references teach the inoculation of a mammalian host with a particulate polynucleotide by direct injection, as specifically recited in Claim 29; methods of transfecting APCs as specifically recited in Claims 68-71; and elicitation of a CTL immune response as specifically recited in the Claim 71. Because the references do not teach all of the elements of the rejected claims, Appellants respectfully submit that the present invention is not anticipated by the references.

On a related matter, the Examiner states that direct injection is clearly taught by Tang and Barry "since the biolistic system requires that DNA be directly injected into skin." The Examiner is apparently equating the biolistic system and direct injection in support of the argument that the art teaches certain of the present methods. In support of the rejection under 35 U.S.C. § 112, however, the Examiner stated that use of a biolistic device and direct injection are distinct. (See last Office Action, page 3, wherein the Examiner states that Appellants' claims should be limited to biolistic approach because no other route of administration, such as direct injection, is supported.) Thus, one argument is being made with regard to rejecting the claims under 35 U.S.C. § 112, but the Examiner makes what appears to be the exact opposite argument in rejecting claims under 35 U.S.C. § 102. Appellants respectfully submit that this is inappropriate.

Claims 1, 15, 29 and 68-71 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Hui et al. (*Journal of Immunological Methods*, 1994). As noted previously by Appellants, and unaddressed by the Examiner, it is unclear whether the Hui reference is appropriately cited under 35 U.S.C. § 102(b). Although the paper bears a publication date of 1994, nothing indicates whether the publication occurred before September 28, 1994, one year before the effective filing date of the current application.

In any event, Hui does not appear to teach every element of the present claims. For example, Hui discusses immunization through thigh muscle and spleen cells, not dendritic cells or any other type of APC. Appellants, in contrast, specifically recite delivery of particulate polynucleotides to the cytoplasm of APCs. This critical distinction alone renders the present invention patentable over the Hui references.

In addition, neither the immunization through the thigh muscle nor the spleen cells appear to stimulate a CTL response. (See page 151, column 2, "The thigh muscles were immunized . . . . After 20 days, no primary anti-H-2K^b CTL activity could be detected in the spleen cells"; and page 152, column 1, "As in the case of genetic immunization via the thigh muscles, the primary anti-H-2K^b activity detected was marginal . . . .") It was only after restimulation *in vitro* that anti-H-2K^b activity was seen. Thus, the methods of Hui do not elicit an immune response in the manner taught by Appellants. Significantly, the thigh muscle and spleen cells of Hui are not antigen presenting cells. Thus, their ability to present antigen through the MHC Class I pathway is questionable. This is supported by the teachings of Hui, in that it was only after restimulation *in vitro*, that anti-H-2K^b activity was seen. In contrast, Appellants' methods elicit an immune response without the need for additional restimulation *in vitro*. Furthermore, Hui does not appear to show that their method has any antitumor or antiviral immunity as claimed in the present methods. Hui reports that only an allo-antigenic response is elicited, and uses an artificial transplantation rejection antigen of questionable relevance to tumor or viral immunity.

Hui is limited to use of a biolistic device, and therefore does not read on the methodology recited in Claim 29, which specifically recites direct injection. Hui clearly fails to teach transduction of APCs, as recited in Claims 68-70, and a method of inducing a CTL response by transfecting APCs as recited in Claim 71. Because several aspects of the presently claimed invention are not taught by Hui, Appellants respectfully submit that the reference is not appropriately recited under 35 U.S.C. § 102(b).

Claims 1-3, 5-17, 19-32, 34-47, 49-61 and 63-71 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Weiner et al. (U.S. Patent No. 5,593,972) in view of either Tang or Barry. Weiner appears to be directed to methods for using naked DNA to elicit an immune response. In addition, Weiner does

not teach the use of DNA vaccines or particulate polynucleotides for use in particle bombardment. A speculative sentence in Weiner, that their methods might have increased efficiency by use of particle bombardment, has been cited as allegedly overcoming the shortcoming of the reference. Appellants respectfully submit that a one-sentence speculation as to a manner in which efficiency may be increased does not render obvious the present invention. Weiner's claimed methods also appear to require the use of bupivacaine in the immunization of a host against a pathogen. Bupivacaine is taught by Weiner as being a cell stimulating agent that promotes and facilitates the uptake of genetic material by a cell (see Weiner, col. 18, lines 39-43). Appellants transfect APCs without the use of transfecting agents. Moreover, it is unclear as to whether Weiner is even targeting APCs. In addition, Weiner teaches integration of the introduced DNA into the chromosomes of the hosts as one means of accomplishing his method (see Weiner, col. 10, line 65 through col. 11, line 4); the present methods do not include such integration. Thus, the relevance of Weiner's methods to Appellants' methods is tenuous at best, since Appellants' methods recite the delivery of particulate polynucleotides to APCs without the use of bupivacaine. Thus, Weiner does not appear to teach or suggest the present methods.

Moreover, the combination of Weiner with Tang and Barry, who are cited as teaching particle bombardment, does not overcome the shortcomings of the primary reference. More specifically, Tang and Barry utilize particle bombardment to elicit an antibody response, not a response through the MHC Class I pathway as recited by Appellants. Thus, combining the teachings of Tang and Barry with those of Weiner might lead one skilled in the art to conclude that use of particle bombardment would result in an antibody response, but would not necessarily lead one skilled in the art to conclude that such methods would result in the elicitation of a response through the MHC Class I pathway.

For a combination of references to be properly applied, the combination must suggest an improvement along the lines of the invention to those skilled in the art. (See, for example, *In re Sernaker*, 217 USPQ 1 (Fed. Cir. 1983), a copy of which is attached at Tab C). Here, Appellants cannot discern any suggestion whatsoever that the combination relied on by the Examiner would lead to the present method for eliciting an antitumor or antiviral response by the MHC Class I pathway through use of particulate polynucleotides coated with DNA expressing an antigenic protein or fragment thereof. There is no teaching in Weiner of the use of particulate DNA, or the introduction of particulate DNA to antigen presenting cells. There is no teaching in either Tang or Barry of the use of particle bombardment to elicit an immune response through the MHC Class I pathway. Therefore, the combination of the references cannot be said to teach Appellants' claimed methods.

For all of the above reasons, Appellants respectfully submit that the claims are allowable over the art of record.

SUMMARY

Appellants respectfully submit that the specification as filed enables the subject matter of the pending claims. In addition, the claims are not indefinite based on the use of the phrase "capable of generating an immune response." Furthermore, none of the references relied on by the Examiner anticipate or suggest the methods of the present invention for the reasons given above. It is respectfully requested, therefore, that the rejection of the pending claims be reversed, and the case remanded to the Examiner for reissue of a Notice of Allowance. Such action is respectfully requested at an early date.

Respectfully submitted,

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APPENDIX

1. An *in vivo* method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) inoculating said mammalian host with said particulate polynucleotide; and,

(d) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway, wherein said presentation of said antigenic protein or protein fragment elicits an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells.

2. The method of Claim 1 wherein said mammalian host is a human.

3. The method of Claim 2 wherein said DNA fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

5. The method of Claim 3 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

6. The method of Claim 5 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

7. The method of Claim 5 wherein said tumor rejection antigen is Melan-A.

8. The method of Claim 5 wherein said tumor rejection antigen is gp100.

9. The method of Claim 5 wherein said tumor rejection antigen is p53.

10. The method of Claim 5 wherein said tumor rejection antigen is CEA.

11. The method of Claim 5 wherein said tumor rejection antigen is HER2/neu.

12. The method of Claim 5 wherein said viral antigen is HIV gp120, HIV gp160.

13. The method of Claim 5 wherein said viral antigen is Influenza virus nucleoprotein.

14. The method of Claim 5 wherein said viral antigen is Hepatitis B surface antigen.

15. An *in vivo* method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) inoculating said mammalian host with said particulate polynucleotide using a biolistic device; and,

(d) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway, wherein said presentation of said antigenic protein or protein fragment elicits an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells.

16. The method of Claim 15 wherein said mammalian host is a human.

17. The method of Claim 16 wherein said DNA fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

19. The method of Claim 17 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

20. The method of Claim 19 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

21. The method of Claim 19 wherein said tumor rejection antigen is Melan-A.

22. The method of Claim 19 wherein said tumor rejection antigen is gp100.

23. The method of Claim 19 wherein said tumor rejection antigen is p53.

24. The method of Claim 19 wherein said tumor rejection antigen is CEA,

25. The method of Claim 19 wherein said tumor rejection antigen is HER2/neu.

26. The method of Claim 19 wherein said viral antigen is HIV gp120, HIV gp160.

27. The method of Claim 19 wherein said viral antigen is Influenza virus nucleoprotein.

28. The method of Claim 19 wherein said viral antigen is Hepatitis B surface antigen.

29. An *in vivo* method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) inoculating said mammalian host with said particulate polynucleotide by direct injection; and,

(d) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell within said mammalian host, such that said expressed antigenic protein or antigenic protein fragment is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway, wherein said presentation of said antigenic protein or protein fragment elicits an anti-tumor or anti-viral immune response in said host that destroys neoplastic or virally infected cells.

30. The method of Claim 29 wherein said mammalian host is a human.

31. The method of Claim 30 wherein direct injection is by subcutaneous injection.

32. The method of Claim 31 wherein said recombinant DNA vector fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

34. The method of Claim 32 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

35. The method of Claim 34 wherein said tumor rejection antigen is selected from the group consisting of MAGE-1 and MAGE 3.

36. The method of Claim 34 wherein said tumor rejection antigen is Melan-A.

37. The method of Claim 34 wherein said tumor rejection antigen is gp100.

38. The method of Claim 34 wherein said tumor rejection antigen is p53.

39. The method of Claim 34 wherein said tumor rejection antigen is CEA.

40. The method of Claim 34 wherein said tumor rejection antigen is HER2/neu.

41. The method of Claim 34 wherein said viral antigen is HIV gp120, HIV gp160.

42. The method of Claim 34 wherein said viral antigen is Influenza virus nucleoprotein.

43. The method of Claim 34 wherein said viral antigen is Hepatitis B surface antigen.

44. An *ex vivo* method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses an antigenic protein or antigenic protein fragment;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell of a mammalian host *in vitro*, such that said expressed antigenic protein or antigenic protein fragment is presented on the membrane surface of said antigen presenting cell through the MHC class I pathway,; and,

(d) inoculating said mammalian host with said antigen presenting cell by direct injection, wherein presentation of said expressed antigenic protein or protein fragment on said antigen presenting cells of said hosts elicits an anti-tumor or anti-viral immune response that destroys neoplastic or virally-infected cells in said host.

45. The method of Claim 44 wherein said mammalian host is a human.

46. The method of Claim 45 wherein direct injection is by subcutaneous injection.

47. The method of Claim 46 wherein said recombinant DNA vector fragment expresses a tumor rejection antigen, viral antigen or antigenic protein fragment thereof.

49. The method of Claim 47 wherein said antigen presenting cells resides within or migrates to the lymphoid tissue of said human host.

50. The method of Claim 49 wherein said tumor rejection antigen selected from the group consisting of MAGE-1 and MAGE 3.

51. The method of Claim 49 wherein said tumor rejection antigen is Melan-A.

52. The method of Claim 49 wherein said tumor rejection antigen is gp100.

53. The method of Claim 49 wherein said tumor rejection antigen is p53.

54. The method of Claim 49 wherein said tumor rejection antigen is CEA.

55. The method of Claim 49 wherein said tumor rejection antigen is HER2/nue.

56. The method of Claim 49 wherein said viral antigen is HIV gp120, HIV gp160.

57. The method of Claim 49 wherein said viral antigen is Influenza virus nucleoprotein.

58. The method of Claim 49 wherein said viral antigen is Hepatitis B surface antigen.

59. An *ex vivo* method of treating a mammalian host capable of generating an immune response, which comprises:

(a) generating a DNA fragment which expresses a molecule which enhances the antigen presentation function of an APC;

(b) distributing said DNA fragment on a particle surface, resulting in a particulate polynucleotide;

(c) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell of a mammalian host *in vitro*, such that said antigen presentation enhancing protein is expressed; and,

(d) inoculating said mammalian host with said antigen presenting cell by direct injection.

60. The method of Claim 59 wherein said mammalian host is a human.

61. The method of Claim 60 wherein direct injection is by subcutaneous injection.

63. The method of Claim 61 wherein said antigen presenting cell resides within or migrates to the lymphoid tissue of said human host.

64. The method of Claim 63 wherein said DNA vector fragment expresses a costimulatory molecule.

65. The method of Claim 64 wherein said costimulatory molecule is selected from the group consisting of CD80 and CD86.

66. The method of Claim 63 wherein said DNA vector fragment expresses a cytokine molecule.

67. The method of Claim 66 wherein said cytokine molecule is selected from the group consisting of IL-12, IL-4 and IL-2.

68. A method for transfecting an antigen presenting cell comprising:

(a) distributing a DNA fragment which expresses an antigenic protein or fragment thereof on a particle surface, resulting in a particulate polynucleotide;

(b) delivering said particulate polynucleotide to the cytoplasm of an antigen presenting cell, such that said expressed antigenic protein or fragment thereof is presented to the membrane surface of said antigen presenting cell.

69. The method of Claim 68, wherein said delivering step occurs *in vivo*.

70. The method of Claim 68, wherein said delivering step occurs *in vitro*.

71. A method of inducing a CTL immune response in a mammalian host capable of generating an immune response, comprising the step of transfecting antigen presenting cells of said host *in vivo* with a DNA fragment which expresses an antigenic protein or fragment thereof, such that said antigenic protein or fragment

thereof is presented to the membrane surface of said antigen presenting cell through the MHC class I pathway and tumor cells are destroyed.

Exhibit A

DNA-based immunization by *in vivo* transfection of dendritic cells

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Delivery of antigen in a manner that induces effective, antigen-specific immunity is a critical challenge in vaccine design. Optimal antigen presentation is mediated by professional antigen-presenting cells (APCs) capable of taking up, processing and presenting antigen to T cells in the context of costimulatory signals required for T-cell activation. Developing immunization strategies to optimize antigen presentation by dendritic cells, the most potent APCs, is a rational approach to vaccine design. Here we show that cutaneous genetic immunization with naked DNA results in potent, antigen-specific, cytotoxic T lymphocyte-mediated protective tumor immunity. This method of immunization results in the transfection of skin-derived dendritic cells, which localize in the draining lymph nodes. These observations provide a basis for further development of DNA-based vaccines and demonstrate the feasibility of genetically engineering dendritic cells *in vivo*.

The goal of vaccination is to induce antigen-specific immunity to protect the host. Current vaccines can elicit effective antibody responses. However, the induction of cytotoxic T-lymphocyte (CTL) responses has been problematic. CTLs are an important component of the immune response to virally infected cells and tumors. CTLs kill neoplastic cells through the recognition of antigenic peptides presented by MHC class I molecules on the surface of the tumor target[1]. These peptides are derived from tumor antigens that are synthesized by the affected cell and degraded in the cytosol of the tumor target[2]. Although the recognition of peptide–class I complexes is sufficient to trigger target cell lysis, priming of CTL responses requires the presentation of the relevant antigen by professional antigen-presenting cells (APCs) capable of providing costimulation. Attempts to induce tumor-specific CTL responses *in vivo* by immunization with killed tumor cells or component proteins have generally been unsuccessful, presumably because proteins in the extracellular fluids cannot enter the cytosol and access the MHC class I presentation pathway.

Genetic immunization has been shown to induce humoral and CTL-mediated immune responses *in vivo*[3–9]. Through genetic immunization, the gene encoding a target antigen can be introduced into the cytoplasm of a cell, resulting in endogenous production of the antigen and presumably MHC class I access. Several *in vivo* gene transfer methods result in significant transgene expression, including retroviral or adenoviral mediated gene transfer and the direct injection of naked DNA.

The mechanism of genetic immunization is unknown[10]. Humoral responses may be explained by the secretion of antigen from transfected somatic cells, or by release of antigen as a result of cell lysis. Exogenous proteins released in this fashion could be taken up and presented to $CD4^+$ T cells by APCs in the draining lymph nodes.

The mechanism of presentation of genetically introduced antigens to $CD8^+$ CTLs is less clear. One possible scenario is that transfected nonprofessional APCs could present the immunogen directly, as transfection would result in endogenous synthesis and MHC class I access. However, this model does not take into account the absence of costimulation, typically provided by professional APCs. Another possibility is that lysis of transfected cells results in the uptake and presentation of antigens associated with cellular debris via phagocytosis by professional APCs. Phagocytosis of antigens allows access to the MHC class I pathway in professional APCs and induction of antigen-specific, CTL-mediated tumor immunity[11,12]. Similarly, it is possible that heat shock proteins could deliver peptides derived from antigens expressed in transfected cells to the MHC class I-restricted presentation pathway of professional APCs (ref. 13). Finally, it is possible that the actual process of genetic immunization directly transfects professional APCs. This would result in endogenous production of antigen within professional APCs and class I presentation in the context of appropriate costimulation for T-cell activation. Though genetic immunization can result in antigen expression by a variety of somatic cells (including myocytes[14] and keratinocytes[15]), the *in vivo* transfection of professional APCs has not been described.

Biolistic delivery of naked DNA is a physical method of DNA delivery, facilitating controlled delivery of DNA without the use of viral vectors[16]. Using gene gun technology, a single cutaneous immunization with as little as 1 μg of DNA can result in significant levels of transgene expression[16]. Because the skin is rich in dendritic cells, we hypothesized that cutaneous bombardment with DNA using the gene gun would result in direct transfection of these cutaneous dendritic cells. In this study we sought to determine the capacity of cutaneous biolistic genetic immunization to elicit protective immunity to lethal tumor challenge and to investigate the mechanism of this form of genetic immunization.

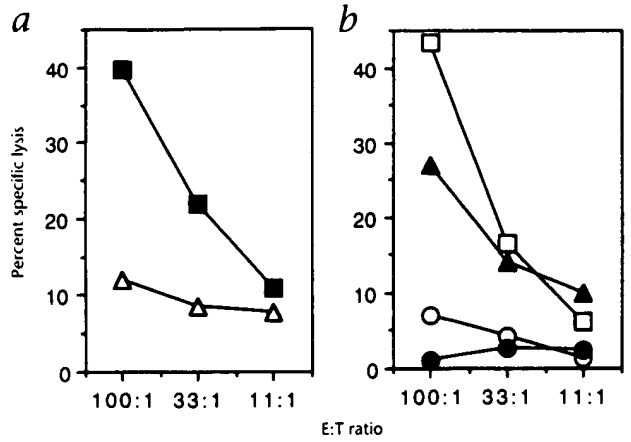

Fig. 1 Immunization by cutaneous delivery of OVA encoding DNA induces OVA-specific CTLs. *a*, *In vitro* restimulated splenocytes from OVA-immunized mice were assayed for cytolytic function against the OVA-transfected lymphoma EG7 (■) or the untransfected parent EL4 (△). *b*, Effector populations were incubated with complement alone (□) or with mAbs against CD4⁺ (▲), CD8⁺ (○), or Thy-1.2⁺ (●) lymphocytes and complement, then assayed for cytolytic activity against EG7 targets. Results are reported as the means of triplicate cultures for the effector:target ratios listed. The s.e.m. of triplicate cultures was always less than 15% of the mean. Experiments were repeated three times with similar results.

Induction of tumor immunity

To determine the potential of genetic immunization to induce protective tumor immunity, we utilized a tumor model consisting of the poorly immunogenic C57BL/6 mouse-derived melanoma B16 (ref. 17), and a subclone engineered to express the foreign antigen protein ovalbumin (OVA)[12]. Foreign antigen genes transfected into tumor cells behave like tumor antigens[12,18–22]. In this model, OVA functions as a defined model tumor antigen. The OVA-transfected B16 subclone MO4 endogenously synthesizes OVA and generates and presents the OVA peptide SIINFEKL with its surface class I molecule K^b (ref. 12). The expression of the OVA antigen does not significantly increase the immunogenicity of this tumor *in vivo*, as tumor growth and progression are similar to that of the untransfected parent[12]. This type of model has been used by numerous investigators to evaluate tumor-specific immunity[12,18–22].

In initial experiments, we evaluated the capacity of biolistic immunization to induce antigen specific CTLs. Naive C57BL/6 mice were immunized with a total of 2.00 μg of OVA encoding DNA delivered to the abdominal skin with two spatially overlapping pulses and boosted in an identical fashion 7 days later. *In vitro* restimulated spleen cells from these mice lysed the syngeneic OVA-expressing murine thymoma EG7, but not the untransfected parent tumor EL4 (Fig. 1*a*). Thus, target cell lysis was antigen specific and dependent on expression of OVA by the tumor target. Depletion of T-cell subsets from the effector populations using monoclonal antibodies demonstrated that lysis depended on Thy-1⁺, CD8⁺ subsets characteristic of MHC class I-restricted CTL effector cells (Fig. 1*b*).

In order to determine the capability of biolistic immunization in inducing protective tumor immunity, groups of mice that were immunized and boosted as described above were challenged 7 days later by intradermal injection of the MO4 or B16 melanoma at a distant site. OVA-immunized mice were protected from lethal tumor challenge, whereas tumors in control mice (immunized similarly, but with naked DNA encoding the irrelevant antigen β-galactosidase) continued to grow and were uniformly lethal by day 34 (Fig. 2*a*). OVA-immunized mice were not protected from challenge with the untransfected parent melanoma B16 (Fig. 2*b*), indicating that protective immunity was antigen specific, depending on OVA expression by the tumor target. We evaluated the contribution of CD8⁺ effector cells to this protective tumor immunity by depleting groups of immunized or control (*lacZ*-immunized) animals of CD8⁺ effector cells through repeated intraperitoneal (i.p.) injection of anti-CD8 monoclonal antibody before tumor challenge[12]. Although OVA-immunized animals were protected from MO4 challenge, survival in immunized, CD8⁺ T cell-depleted animals was similar to that observed in control animals, with or without T-cell depletion (Fig. 2, *c* and *d*). Therefore, CD8⁺ T cells are essential for the protective tumor immunity induced by genetic immunization in this model.

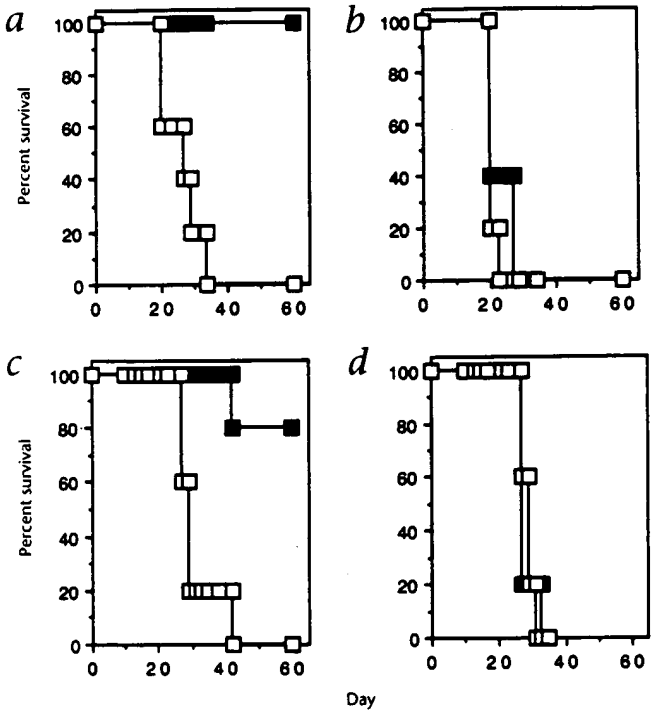

Fig. 2 Immunization by cutaneous delivery of OVA encoding DNA induces antigen-specific, CTL-mediated protection from lethal challenge with the OVA expressing melanoma MO4. Mice were genetically immunized with OVA (■) or *lacZ* (□) and boosted 7 days later. Groups of immunized mice were challenged 7 days after the final immunization (day 0) with either the B16 melanoma (*b*) or the OVA expressing subclone MO4 (*a*). Alternatively, immunized mice were divided into two groups, one of which was depleted of CD8⁺ lymphocytes by i.p. injection of anti-CD8 mAb 7 and 9 days after the last immunization. Intact (*c*) and CD8⁺ depleted (*d*) mice were then challenged 10 days after the final immunization (day 0) with MO4. Survival was reported as the percentage of surviving animals. Animals surviving on day 60 had no sign of tumor growth. All experiments included five mice per group and were repeated at least three times. Mice that became moribund were killed according to animal care guidelines.

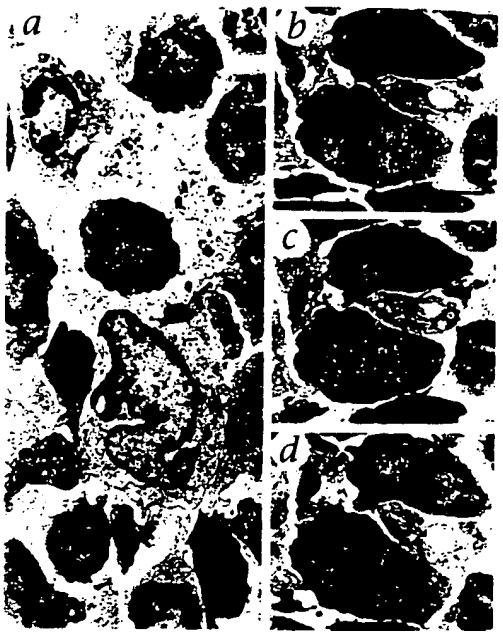

Fig. 3 Presence of particles in dendritic cells within lymph nodes draining the site of immunization. Mice were immunized as described in Fig. 1. Animals were killed 24 hours later, and draining lymph nodes were harvested and processed as described in the Methods section and observed using a JEOL 100CX microscope. *a*, A dendritic cell containing a single gold particle within the cytoplasm may be seen. Morphologic indices were used to confirm the identity of the cell; principally these are size, a paucity of cytoplasmic granules, and the presence of cytoplasmic veils. To confirm the cytoplasmic locale of the gold particles, serial sections were cut. It can be seen in *b–d* that the presence of the gold particles continues throughout all three sections (separated by 150 nm).

Transfection of dendritic cells *in vivo*

To investigate the mechanism of immunization in this model, we immunized naive C57BL/6 mice with a total of 2.00 μg of plasmid DNA encoding the Lantern variant of the reporter gene for green fluorescent protein (GFP). This gene encodes a naturally fluorescent protein requiring no substrate for visualization. DNA-coated particulates were constructed and delivered by the same techniques used for OVA immunization. Draining lymph nodes of immunized mice were excised and sectioned 24 hours after immunization. Electron microscopic analysis revealed cells within the lymph nodes with dendritic cell form and structure that appeared to contain 1-μm electron-dense particles (Fig. 3*a*). Serial sections demonstrated intracytoplasmic locale of the particles (Fig. 3, *b–d*). To confirm expression of the delivered GFP genes, cytospins of single-cell suspensions from draining lymph nodes excised 24 hours after immunization were examined by fluorescence microscopy. Green fluorescence in cells from GFP-immunized mice indicated selective expression of GFP (Fig. 4*a*) in cells with dendritic cell form and structure. Differential interference contrast imaging shows the positively staining cells to have a dendritic cell form and structure (Fig. 4*b*), consistent with the electron microscopic studies. Furthermore, gold particles could be detected in these cells quite easily under bright-field microscopy (Fig. 4, *b–d*). Lymph node cells from control mice, identically immunized with particles coated with irrelevant plasmid, contained particles but did not fluoresce (data not shown). Together, these results demonstrate expression of genetically introduced protein by particle-containing dendritic cells in the draining lymph nodes.

Transfected dendritic cells are derived from the skin

In order to determine the origin of the transfected dendritic cells, the shaved abdomens of naive mice were painted with rhodamine immediately before biolistic immunization with GFP. This treatment labels cutaneous dendritic cells and facilitates analysis of cutaneous dendritic cell trafficking to the regional lymph nodes[23,24]. Twenty-four hours after immunization, draining lymph nodes were excised and sectioned for analysis. Clusters of skin-derived cells (red fluorescence) were evident within the lymph nodes in the region of afferent lymph flow (Fig. 5*a*). Overlays of green fluorescence (GFP expression) revealed several double-positive cells, demonstrating GFP expression in skin-derived dendritic cells within the draining lymph node (Fig. 5*b*).

Discussion

Genetic immunization is an attractive approach for the induction of viral or tumor immunity. Vaccination with naked DNA can induce both humoral and cell-mediated immune responses and protection against viral infection or tumor challenge. Naked DNA-based vaccines offer several potential advantages over viral mediated transduction[9,10]. Among these is the potential for rapid and inexpensive production of large-scale DNA preparations. Such vaccine preparations can be prepared with relative purity and would be significantly more stable than current protein-based vaccines. Furthermore, the use of naked DNA vaccines would be inherently safer than viral mediated gene transfer, particularly in a potentially immunocompromised host. In addition, the use of naked DNA would eliminate immune responses to viral carriers, which can result in rapid elimination of transduced cells or limit the effectiveness of readministration.

Genetic immunization induces tumor-specific immunity. Several studies have shown that immunization with naked DNA against either natural or model tumor antigens can induce immunity to tumors expressing the antigen gene. A variety of strategies are being investigated to optimize this form of immunization. Recently, Conroy *et al.* have shown that predelivery of DNA encoding granulocyte-macrophage colony-stimulating factor (GM-CSF) augmented carcinoembryonic antigen (CEA)-specific immunity induced by cutaneous particle bombardment with CEA encoding DNA (ref. 25). In another variation, Ciernik *et al.* have shown that biolistic genetic immunization with a minigene encoding a single epitope from mutant p53 targeted to the endoplasmic reticulum was partially able to protect mice from p53-expressing tumors[26]. Furthermore, Irvine *et al.* have shown regression of β-galactosidase-expressing tumors when gene gun immunization with the gene encoding β-galactosidase is carried out in combination with adjuvant cytokine therapy[27].

Current attempts to optimize naked-DNA immunization are proceeding without a clear understanding of the mechanism of this form of immunization. In this report, we address the mechanism of biolistic cutaneous genetic immunization. This method of naked-DNA immunization has been shown to be several times more efficient than other forms of inoculation[9]. We hypothesized that the effectiveness of this method may be in part due to the presence of significant numbers of dendritic cells in the tar-

get tissue. The skin is rich in dendritic cells, and these dendritic cells are capable of migrating to the regional lymph nodes where they exhibit potent APC function[23,24].

Our results demonstrate that biolistic genetic immunization induces potent antigen-specific CTL responses and antigen-specific, CTL-dependent protective tumor immunity. To show this we have used the nonimmunogenic murine melanoma B16 and a transfected subclone expressing the model tumor antigen OVA. The expression of the OVA antigen does not significantly increase the immunogenicity of this tumor *in vivo*, as tumor growth and protection are similar to that of the untransfected parent[12]. In our model OVA is endogenously synthesized by the transfected melanoma, and the SIINFEKL epitope is generated and presented with the class I molecule K^b on the surface of transfected cells[12]. In this respect, the nonself antigen OVA behaves as do many "natural" tumor antigens that are derived from viruses or mutated "altered-self" host proteins. It should be noted, however, that several identified tumor antigens are derived from nonmutated self antigens and that additional investigations will be needed to determine whether conclusions derived from nonself models are as applicable to such "autoantigens." Nevertheless, because the biology of the processing and presentation of antigen in this model is the same as that of many naturally occurring nonself tumor antigens, results from this model should be applicable to a wide variety of human tumors. The use of this well-defined model and others like it[18–21,27] is important for studies designed to define and optimize critical parameters for tumor immunization and will also facilitate direct comparisons between alternative immunization strategies[12,22].

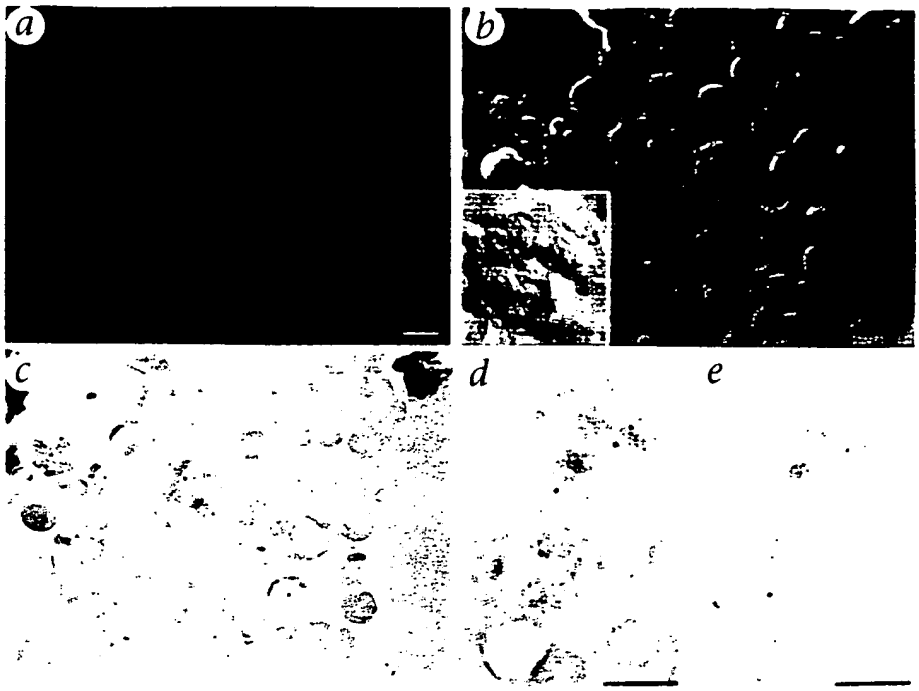

Fig. 4 Expression of introduced protein by genetically engineered, particle-containing dendritic cells in the draining lymph nodes. Mice were immunized as described in Fig. 1 except that particles were coated with the pGREEN LANTERN-1 plasmid (Gibco BRL), which contains the "humanized" reporter gene encoding GFP from the *Aequorea victoria* jellyfish. GFP is a naturally fluorescent protein. Draining lymph nodes were excised 24 h after immunization. Cytospins of lymph nodes were used to detect GFP-positive cells by fluorescence microscopy as described in Methods. Observation was with a Nikon photomicroscope using a 60X 1.4NA plan-apochromatic objective. *a*, The green fluorescent protein image is shown, signal from the GFP is clearly restricted to the cells central within the field (arrows). *b*, The differential interference contrast microscope image of the same fields shows the two cells to be dendritic (arrows), surrounded by smaller round lymphocytes. *b, inset*, At higher power gold particles may be visualized. *c*, The presence of the gold particles is more clearly detected using bright-field imaging (arrows). *d* and *e*, In fact, gold particles are detected in both GFP-positive cells at different focal planes (scale bar, 10 mm). Similarly prepared sections from naive animals do not demonstrate these distinctly colored, uniform beads.

Mechanism of biolistic genetic immunization. Our results show that biolistic cutaneous genetic immunization results in the presence of bombarded projectiles in the cytoplasm of dendritic cells in the draining lymph nodes. Identical delivery of DNA encoding the marker protein GFP demonstrates that introduced genes can be expressed as proteins by particle-containing dendritic cells in the lymph nodes. This is the first demonstration of *in vivo* transfection of dendritic cells that we are aware of. That these dendritic cells are skin-derived is demonstrated by the presence of double-stained skin-derived dendritic cells (red fluorescence) expressing GFP (green fluorescence) in tissue sections of the draining lymph node.

In combination, the data presented here support the hypothesis that biolistic immunization results in delivery of DNA to cutaneous dendritic cells. Thereafter, transfected dendritic cells migrate to draining lymph nodes, as they do for the presentation of protein and hapten antigens. Endogenously synthesized antigen can access the MHC class I-restricted pathway of transfected dendritic cells and can be presented to T cells in the lymphoid tissue with appropriate costimulatory signals for T-cell activation. Our studies do not rule out the possibility that DNA-coated beads may travel through the lymphatics to the lymph nodes where they may be directly captured by resident dendritic cells. In this regard, recent studies suggest that immature dendritic cells capable of particulate phagocytosis exist in the hepatic lymph and spleen[28], and our previous studies and others[11,12] suggest that subcutaneously administered particle-associated antigens can access the cytosol of phagocytic cells through a phagosome-to-cytosol pathway *in vivo*. It is unclear whether *in vivo* administered particle-bound naked DNA could survive trafficking to the lymph nodes, uptake by resident dendritic cells, and endosomal transport and escape and still be functionally expressed. We believe this would be unlikely in this system, as DNA coated onto gold beads by this method is rapidly solubilized in aqueous media with greater than 95% of the DNA dissociating from the beads in less than 3 min (data not shown). It is possible that such solubilized DNA may traffic to the regional lymph

nodes and be taken up and expressed by resident dendritic cells independently of the beads, but it is unlikely that this mechanism alone would account for the colocalization of gene expression and particles within cells, the transfection of skin-derived dendritic cells, and the high efficiency of transfection we observe.

In common with previous reports[14,15], we also observe antigen expression in nonprofessional APCs at the site of immunization (data not shown). It is possible that antigen released by these cells could indirectly be taken up by APCs and subsequently presented to T cells as well. Elegant studies by Huang *et al.* demonstrate that CTL induction by such "cross-priming" alone would require some mechanism for antigen access to the TAP-dependent classical MHC class I-restricted processing pathway[29]. The direct transfection of dendritic cells would explain the remarkable efficiency of this form of immunization.

It is unclear whether CTL induction by genetic immunization is helper cell dependent. These studies demonstrate that $CD8^+$ CTLs are the predominant effector cells in the protective tumor immunity we observe, but do not address the role of $CD4^+$ T cells in CTL induction. Dendritic cells have an exceptional ability to stimulate naive $CD4^+$ T cells, and several studies have shown that cutaneous biolistic genetic immunization elicits helper cell-dependent antibody responses[3,6,15], presumably by MHC class II-restricted presentation of exogenous antigen released from transfected cells[10]. Recent studies suggest that induction of CTLs by dendritic cells pulsed with MHC class I-restricted peptides requires the presentation of MHC class II-restricted epitopes and activation of $CD4^+$ T cells[30,31]. In contrast, studies by Ciernik *et al.* have shown induction of CTLs by gene gun immunization with DNA encoding only a class I-restricted T-cell epitope[26]. Although the OVA construct used in our studies includes $CD4^+$ T-cell epitopes, our experiments do not directly address whether CTL induction is helper cell dependent in this model.

Currently there is significant interest in the potential use of dendritic cells as adjuvants for immunization. Dendritic cells can be expanded *in vitro*, loaded with diverse forms of antigens including peptides, proteins, and antigen-encoding genes, and reinjected into the host[22,32-34]. Our results demonstrate that dendritic cells can be transfected *in vivo*, potentially obviating the need for *in vitro* expansion, manipulation and reinfusion. This finding also raises the possibility that dendritic cells could be engineered *in vivo*, through the genetic cointroduction of antigens and immunoregulatory molecules, to induce or suppress antigen-specific immune responses in the host.

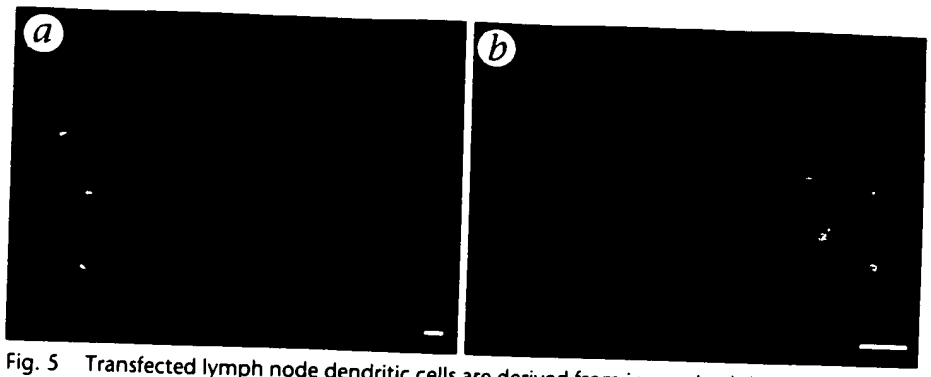

Fig. 5 Transfected lymph node dendritic cells are derived from immunized skin. To detect the presence of skin-derived dendritic cells and the presence of GFP within these cells, lymph nodes from mice painted with rhodamine immediately before immunization with GFP were harvested, fixed in 2% paraformaldehyde in PBS, cryoprotected in 30% sucrose, and shock frozen. Cryosections (5 μm) were cut through the belly of the node and immediately mounted and observed as described in the Methods. *a*, At low power, the skin-derived cells within the node are detected with a rhodamine cube set. It was notable that the majority of the cells occurred in large islands, generally located at the periphery of individual nodes [in this image the edge of the node is delineated (arrows)]. When the rhodamine signal (reflecting skin-derived dendritic cells) and the GFP signal (reflecting positive transfection and active production of GFP) are superimposed, it is clear that many of the red dendritic cell profiles also produce an abundant GFP signal, seen as a yellow signal in *b*. Occasional profiles that contain predominantly green signal are present in this image. This is considered to reflect cells that either were successfully transfected with GFP, although they were not stained by the topical rhodamine, or the cell section is at the limit of the cytoplasm such that some GFP signal occurs but none of the predominantly plasmalemmal rhodamine is detectable. Scale bar, 25 μm. Rhodamine signal is absent in unpainted animals.

Methods

Mice and cell lines. Female C57BL/6 mice, 5–8 weeks old, were purchased from the Jackson Laboratories (Bar Harbor, Maine). EL4 is a C57BL/6 T lymphoma, and EG7 is a chicken egg ovalbumin (OVA)-transfected subclone of EL4 (ref. 21, kindly provided by M. Bevan). The C57BL/6-derived murine melanoma B16 (ref. 17) was obtained from the American Type Culture Collection [(ATCC), Rockville, Maryland]. MO4 was constructed by transfection of B16 with the pAc-neo-OVA plasmid as described[12]. Monoclonal antibodies were prepared from the hybridomas GK1.5 (anti-CD4, ATCC TIB-207), 2.43 (anti-CD8, ATCC TIB-210) or 30-H12 (anti-Thy-1.2, ATCC TIB-107). Ascites containing anti-CD8 antibodies was raised in BALB/c *nu/nu* mice by i.p. injection of GK1.5 cells (3×10^6) and incomplete Freund's adjuvant (0.5 ml per mouse).

Genetic immunization. Genetic immunization was accomplished by biolistic bombardment using methods similar to those recently described[25]. Briefly, DNA-coated gold particles were prepared by combining 50 mg of 0.95 μm gold beads and 100 μl of 0.1 M spermidine and sonicating for 5 s. Plasmid DNA (100 μg) and $CaCl_2$ (200 μl) were added sequentially to the beads spinning in a vortex mixer. This mixture was allowed to precipitate at room temperature for 5–10 min. The bead preparation was then centrifuged (10,000 r.p.m. for 30 s) and washed 3 times in cold ethanol before resuspension in 7 ml of ethanol to give a final concentration of 7 mg gold per milliliter. The solution was then loaded into Tefzel tubing (Agracetus, Middleton, Wisconsin) and allowed to settle for 5 min. The ethanol was removed and the beads were attached to the sides of the tubing by rotation at 20 r.p.m. for 30 s and N_2 dried. The dry tubing lined with beads was then cut into 0.5-inch sections and stored for use with desiccant in parafilm-sealed vials. Animals were vaccinated by delivery of two shots (each shot consisted of 0.5 mg gold beads in 0.5 inch of tubing) to the shaved abdominal region using the *Accell* gene delivery device (Agracetus) at a discharge pres-

sure of 400 p.s.i. This delivers approximately 1.00 μg/DNA per shot. Animals were immunized with either the pAc-neo-OVA plasmid[21] or the pIEglacZ plasmid (kindly provided by L. Huang), which contains the *lacZ* gene under the control of the CMV promoter. In some experiments, mice were immunized as described except that particles were coated with the pGREEN LANTERN-1 plasmid (Gibco BRL, Gaithersburg, Maryland), which contains the "humanized" reporter gene encoding GFP from the *Aequorea victoria* jellyfish. This gene encodes a naturally fluorescent protein requiring no substrates for visualization.

Cytotoxicity assays. Splenocytes from immunized animals were restimulated with minor modifications of previously described protocols[12]. Briefly, 1 week after immunization, splenocytes (30×10^6) were restimulated by coculture with irradiated (20,000 rad) EG7 cells (10×10^6). Effector cells were harvested 5 days later and cultured with 2×10^4 ^{51}Cr-labeled targets in round-bottom microwells (200 μl) at the indicated effector:target cell ratio. In some cases the effector cells were depleted of T-cell subsets using mAb plus complement before assay as described[22]. After 4 h at 37 °C, 100 μl supernatant from triplicate microcultures was collected and counted, and the percentage of specific release was calculated as described[12]. Results are reported as the mean of triplicate cultures. The s.e.m. of triplicate cultures was always less than 15% of the mean.

Protection assays. C57BL/6 mice were immunized as described with the indicated antigen–gene construct. Animals were challenged with tumors and evaluated for tumor survival as described[12]. Briefly, 7 days after the final immunization (day 0), OVA-immunized or *lacZ*-immunized animals were challenged by intradermal injection in the mid-flanks bilaterally with melanoma cells (2×10^4) at two times the dose lethal to 50% of the animals tested (LD_{50}). Survival is recorded as the percentage of surviving animals. Melanoma cells for injection were washed three times in PBS. Injected cells were greater than 95% viable by trypan blue exclusion. All experiments included five mice per group and were repeated at least three times. Mice that became moribund were killed according to animal care guidelines of the University of Pittsburgh Medical Center. In some experiments, animals were depleted of $CD8^+$ cells. This was accomplished by i.p. injection of CD8 mAb (2.43) 7 and 9 days after immunization as described, followed by tumor challenge on day 10 (ref. 12).

Electron microscopy. For electron microscopy, 24 h after immunization animals were killed, and draining lymph nodes were harvested and fixed in 2.5% glutaraldehyde for 1 h. Following fixation, nodes were washed in PBS, diced into 1-mm cubes, postfixed for 1 h in 1% aqueous osmium tetroxide, dehydrated through graded alcohols and embedded in Epon (Energy Beam Sciences, Waltham, Massachusetts). Following embedment, thin (60-nm) sections were cut using a Reichert Ultracut S (Leica, Chicago, Illinois) microtome, mounted on copper grids, counterstained with 2% uranyl acetate (7min) and 1% lead citrate (2 min), dried and observed using a JEOL 100CX microscope (JOEL, Chicago, Illinois). Morphologic indices were used to confirm the identity of the cell, principally these are size, a paucity of cytoplasmic granules, and the presence of cytoplasmic veils. To confirm the cytoplasmic locale of the gold particles, serial sections were cut (separated by 150 nm).

Fluorescence microscopy. Mice were immunized as described in Fig. 1 except that particles were coated with the pGREEN LANTERN-1 plasmid, which encodes GFP. Draining lymph nodes were excised 24 h after immunization.

Cytospins of lymph nodes were used to detect GFP-positive cells by fluorescence microscopy. Cells were centrifuged at 500 r.p.m. for 5 min, and mounted directly in an aqueous mounting medium (Gelvatol, Monsanto). Observation was with a Nikon FXL (Chicago, Illinois) photomicroscope using a 60X 1.4NA plan-apochromatic objective. All images were collected digitally using a Sony 3 chip color camera. In the case of fluorescence images, three individual frames were integrated to obtain an optimally contrasted image.

In order to detect the presence of skin-derived dendritic cells and the presence of GFP within these cells, lymph nodes from mice painted with rhodamine immediately before immunization were harvested, fixed in 2% paraformaldehyde in PBS, cryoprotected in 30% sucrose, and shock frozen. Cryosections (5 μm) were cut through the belly of the node, mounted on Superfrost slides (Fisher, Pittsburgh, Pennsylvania) and kept frozen until observation. Following removal from the cryostat chamber, sections were immediately mounted and observed, as described above. At low power, the skin-derived cells within the node are detected with a rhodamine cube set.

Acknowledgments

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Exhibit B

The PTO operates in accordance with detailed rules and regulations, including those set out in the Manual of Patent Examining Procedure (MPEP) which is made available to the public and which has been held to describe procedures on which the public can rely. In re Kaghan, 387 F.2d 398, 401, 156 USPQ 130, 132 (CCPA 1967). Our standard for review is whether the rule or procedure is within the agency's statutory authority and is reasonably related to the purposes of the enabling legislation, Mourning v. Family Publications Service, Inc., 411 U.S. 356, 369 (1973), and does no violence to due process. Mathews v. Eldridge, 424 U.S. 319 (1976). The rules and procedures here challenged all relate to the threshold decision by the PTO of whether to reexamine Gould's patents.

A. MPEP §2286

MPEP §2286 provides that the PTO will not stay its reexamination of a patent that is in litigation unless trial has commenced. As discussed ante, Gould asserts that this practice is directly contrary to the legislative purpose of providing an expeditious alternative to the entire process of litigation. Gould argues that in this case Congress' intention was defeated by the PTO's refusal to stay reexamination. He asserts that MPEP §2286, whereby the PTO proceeded with reexamination of Gould's patents, is contrary to statutory authority and invalid, and reexamination of Gould's patents should be vacated.

The Commission responds that it is not for the PTO to decide whether trial will continue to be stayed, and takes issue with Gould's statement that the completion of pre-trial procedures is a sufficient assurance of imminent trial as to require the PTO to refrain from proceeding with a request for reexamination, even if proceeding with such request would delay the trial, as occurred in Gould's situation. The PTO also argues that the rule is in accord with the statute.

Essentially, Gould argues that the PTO should be required to exercise discretion on whether to proceed with reexamination in view of imminent trial, and that the failure to authorize and to exercise such discretion is a critical flaw in PTO practice, which alone or with other flaws requires us to vacate the reexamination process that Gould's patents are undergoing.

We find no merit in Gould's analogy to reissue practice, for we observe that PTO procedures are identical for both reissue and reexamination applications where a court has stayed litigation, see MPEP §1442.03, suggested Form Paragraph 14.07:

> While there is concurrent litigation related to this reissue application, action in this reissue application will NOT be stayed because a stay of that litigation is in effect for the purpose of awaiting the outcome of these reissue proceedings.

See also 37 C.F.R. 1.565(b).

Even if PTO discretion to stay reexamination were authorized it could not affect Gould's situation. The Florida district court did not invite the PTO to exercise discretion on whether to consider Control Laser's reexamination request, and did not defer to the PTO to decide whether reexamination or trial should proceed first. The Florida court itself stayed the trial in order for reexamination to be pursued. (The stay of pending litigation to enable PTO review of contested patents was one of the specified purposes of the reexamination legislation.) The court never relinquished control of its right to proceed with the trial; and the PTO never was granted the right to decide whether or when trial would proceed.

[3] On these facts, the PTO did not have the opportunity to exercise the discretion that Gould complains MPEP §2286 prevents it from exercising. Whatever deprivation Gould may be experiencing due to the ongoing reexamination is not due to this administrative procedure, and we find no due process question raised thereby. Nor do we find in §2286 a derogation of the statutory purpose nor an undue extension of statutory authority. We affirm the district court on this issue.

B. 37 C.F.R. §§1.530(a) and 1.26(c) and MPEP §§2240 and 2244

Gould challenges the lawfulness of 37 C.F.R. §1.530(a), which provides that no statement by a patentee shall be considered by the PTO during the three-month period set in 35 U.S.C. §303 wherein the PTO is required to decide whether any substantial new question of patentability is raised. This objection is presented in the context of the PTO's "rule of doubt" expressed in MPEP §§2240 and 2244.[12] Gould argues that the procedure is flagrantly unfair, since the PTO must rely solely on the representations of the person who requests reexamination without opportunity for any explanation by the patentee. The statute does not prohibit such explanation, but 35 C.F.R. §1.530(a) does. Gould asserts that the deprivation of the opportunity to be heard at this threshold stage violates due process.

Gould also protests 37 C.F.R. §1.26(c), arguing that the $1,500 fee for reexamination unlawfully weights the PTO's initial decision in favor of granting reexamination, because only if reexamination is granted will the PTO avoid refunding $1,200 of the $1,500.

Gould conceded before the district court, for the purpose of this case, that a substantial new question of patentability had been raised in the requests for reexamination of the two patents here at issue. Thus the challenged procedures of 37 C.F.R. §§1.530(a) and 1.26(c), and MPEP §§2240 and 2244, did not apply to Gould's detriment. In the absence of justiciable controversy with respect to these provisions, Gould does not have standing to challenge them. Warth v. Seldin, 422 U.S. 490 (1975); Baker v. Carr, 369 U.S. 186, 204 (1962).

VII

In summary, we affirm the decision of the district court that 35 U.S.C. §§301-307, as applied retroactively to Gould's issued patents, do not violate the Fifth Amendment or the Seventh Amendment or Article III; that 35 U.S.C. §282 does not apply to reexamination; and that MPEP §2286 does not violate statutory and constitutional restraints. The decision of the district court that 37 C.F.R. §§1.26(c) and 1.530(a), and those portions of MPEP §§2240 and 2244 that impose a rule of doubt on the decision to reexamine, do not violate statutory and constitutional restraints is vacated in view of Gould's lack of standing to raise these issues.

Each party will bear its own costs.

Affirmed in Part and Vacated in Part.

[12] The pertinent provisions are:

35 U.S.C. §303(a). Within three months following the filing of a request for reexamination ° ° ° the Commissioner will determine whether a substantial new question of patentability affecting any claim of the patent concerned is raised by the request ° ° ° °

37 C.F.R. §1.530(a). [N]o statement or other response by the patent owner shall be filed prior to the determinations made ° ° ° °. If a premature statement or other response is filed by the patent owner it will not be acknowledged or considered in making the determination.

MPEP §2240. Where doubts exist, all questions should be resolved in favor of granting the request ° ° ° °

MPEP §2244. Any question as to whether a substantial new question of patentability exists should be resolved in favor of granting the request for reexamination.

Court of Appeals, Federal Circuit

Jamesbury Corp. v. Litton Industrial Products, Inc.

No. 84-1079

Decided Mar. 12, 1985

PATENTS

1. Pleading and practice in courts — Jury trial — In general (§53.571)

Instruction, charging jury to give "careful scrutiny" to claimed invention before "endorsing patent monopoly," incorrectly suggests that jury must affirmatively find patent valid, is likely to be prejudicial, and cannot be approved.

2. Pleading and practice in courts — Jury trial — In general (§53.571)

Jury instructions, to effect that claims are invalid if prior art discloses "substantially the same thing" as claims, and which speak of claims not differing "in significant particulars," are not legally correct interpretation of statutory requirement of novelty, since anticipation is not shown by prior art disclosure that is only "substantially the same" as claimed invention, nor is legal standard of such instructions corrected by court's speaking of prior art disclosing claimed invention "in complete terms."

Particular patents — Valves

2,945,666, Freeman, Ball Valve, holding of invalidity of claims 7 and 8 reversed.

Appeal from District Court for the District of Connecticut, Blumenfield, J.

Action by Jamesbury Corp., against Litton Industrial Products, Inc., for patent infringement. From judgment for defendant, plaintiff appeals. Reversed and remanded.

See also 195 USPQ 65, 196 USPQ 544, and 199 USPQ 641.

Robert C. Miller, and Oblon, Fisher, Spivak, McClelland, and Maier, P.C., both of Arlington, Va. (Arthur I. Neustadt, Arlington, Va., on the brief) for appellant.

Donald R. Dunner, and Finnigan, Henderson, Farabow, Garrett & Dunner, both of Washington, D.C. (Allen M. Sokal, and Finnigan, Henderson, Farabow, Garrett & Dunner, both of Washington, D.C., of counsel, and Spencer T. Smith, Hartford, Conn., on the brief) for appellee.

Before Nies, Newman, and Bissell, Circuit Judges.

Nies, Circuit Judge.

Jamesbury Corp., the plaintiff below, charged Litton Industrial Products with infringing claims 7 and 8 of its U.S. Patent No. 2,945,666 to Freeman entitled "Ball Valve."[1] Following a seven day jury trial, the jury returned a verdict for Litton, concluding, in answer to an interrogatory, that the asserted claims did not differ in any "significant particulars" from the prior art.[2] Under the court's instructions, this finding meant that the claims were invalid under 35 U.S.C. §102(a)[3] for lack of novelty. Jamesbury had timely objected to the jury charge on the issue of novelty and to the wording of the particular interrogatory under review, as well as to other instructions. No instructions were given with respect to obviousness of the claimed inventions, Litton having agreed that obviousness was not asserted as a ground for holding the claims invalid. Following entry of judgment, Jamesbury filed a motion under Fed. R. Civ. P. 50(b) for judgment notwithstanding the verdict, which was denied by the district court. In ruling on the motion, the district court stated:

> The jury returned a verdict for the defendant in this patent infringement suit. The plaintiff has moved for judgment notwithstanding the verdict. The plaintiff is seeking judgment on all disputed issues: the validity of the patent, infringement of the patent, the amount of damages, and the defenses of laches and estoppel.
>
> In its response to a special interrogatory, the jury made explicit its finding that the patent was invalid because of lack of novelty over the prior art. Thus the crucial issue to be resolved is whether the jury's finding of invalidity should be set aside. Judgment n.o.v. should only be granted when:
>
> (1) there is such a complete absence of evidence supporting the verdict that the jury's findings could only have been the result of sheer surmise and conjecture, or
>
> (2) there is such an overwhelming amount of evidence in favor of the movant that reasonable and fair minded men could not arrive at a verdict against him.
>
> Mattivi v. South African Marine Corp., 618 F.2d 163, 168 (2d Cir. 1980).
>
> Neither of the tests for judgment n.o.v. is satisfied by the plaintiff's motion. The plaintiff alleges that the defendant has produced no evidence regarding the level of ordinary skill in the ball valve art. Although such proof is essential to support a finding of invalidity because of obviousness, see Environmental Designs v. Union Oil Co., 713 F.2d 693, 695, 218 USPQ 865, 867-68 (Fed. Cir. 1983), the plaintiff has cited no authority requiring such proof to support a finding of invalidity because of lack of novelty over the prior art. On the issue of novelty, there was ample evidence to support the jury's verdict; there was certainly not an overwhelming amount of evidence in the plaintiff's favor that reasonable and fair minded men could not arrive at a verdict against it.
>
> For the foregoing reasons, the motion for judgment n.o.v. is denied.

In this appeal, Jamesbury argues that because of erroneous and prejudicial error in the instructions to the jury, it is entitled at least to a new trial. Jamesbury further asserts that because lack of novelty was not established and other grounds asserted for holding the claims invalid, namely, obviousness and inequitable conduct, were withdrawn or waived, the court erred in its ruling on Jamesbury's motion JNOV. We agree and, therefore, reverse the holding of invalidity of claims 7 and 8. The case is remanded for resolution of other issues.

II.

The standard of review of instructions is prejudicial legal error. Railroad Dynamics, Inc. v. A. Stucki Co., 727 F.2d 1506, 1512, 220 USPQ 929, 939 (Fed. Cir. 1984).

A.

Jamesbury first attacks the following instruction which laid the foundation for the jury's deliberations:

> [T]he public is a silent but nevertheless an important, and interested party in all patent litigation and it is entitled to protection against the monopolization of what is not lawfully patentable. In other words, it's not simply between Jamesbury and Litton. Other people are affected by it.
>
> So I charge you that it is your duty to *subject the invention* defined in claims seven and eight of the Freeman patent *to careful scrutiny before endorsing Jamesbury's right to the patent monopoly* defined by such claims. [Emphasis added.]

Jamesbury argues that the effect of this instruction was to create a presumption of invalidity requiring Jamesbury to prove, beyond careful scrutiny, that it was entitled to maintain a monopoly, which, impliedly, was against the public interest. We agree that this instruction is legally erroneous and prejudicial.

[1] The language that the jury must give "careful scrutiny" before "endorsing" the "patent monopoly" cannot be approved. While the language does not rise to the level of a presumption of invalidity, it does incorrectly suggest that the jury must affirmatively find the patent valid, which is never appropriate. See Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984)("court never 'declares' a patent valid").

Further, this court has disapproved of a challenger's characterization of a patentee by the term "monopolist," which is commonly regarded as pejorative. Union Carbide Corp. v. American Can Co., 724 F.2d 1567, 1574, 220 USPQ 584, 590 n.4 (Fed. Cir. 1984); Carl Schenck A.G. v. Nortron Corp., 713 F.2d 782, 784, 218 USPQ 698, 699 (Fed. Cir. 1983). In both of the cited cases, a bench trial was involved. Here, not only was Litton's counsel not admonished for so characterizing Jamesbury before the jury, a more serious impropriety than in a bench trial, but also the characterization found its way into the instructions. As stated in Connell v. Sears, Roebuck & Co., 722 F.2d 1542, 1548, 220 USPQ 193, 198 (Fed. Cir. 1983), the characterization of a patent as a "monopoly" is misdirected:

> The phrase "patent monopoly" appears at various points. Under the statute, 35 U.S.C. §261, a patent is a form of property right, and the right to exclude recognized in a patent is but the essence of the concept of property. Schenck v. Nortron Corp., 713 F.2d 782, 218 USPQ 693 (Fed. Cir. 1983).

Instructions which supplement the statutory body of law governing patent validity by interjecting language to the effect that the public must be "protected" against a "monopoly," a term found nowhere in the statute, are likely to be prejudicial and should be avoided.

B.

This court has repeatedly held that the facts leading to a conclusion of invalidity must be established by clear and convincing evidence. See, e.g., American Hoist & Derrick Co. v. Sowa & Sons, Inc., 725 F.2d 1350, 1360, 220 USPQ 763, 771 (Fed. Cir. 1984) and its progeny. This standard is unvarying. Therefore, Jamesbury correctly asserts that error was committed by the district court in giving the following instruction to the jury:

> If you find that to be so *by a preponderance of the evidence*, that the Saunders British patent or other prior art disclosed substantially the same things as set forth in Freeman's claims 7 and 8 and in the same scope as here asserted for infringement purposes, then such claims 7 and 8 are void for lack of novelty. [Emphasis added.]

---

[1] This case has been twice before the United States District Court for the District of Connecticut, and once before the United States Court of Appeals for the Second Circuit. Jamesbury Corp. v. Litton Industrial Products, Inc., 442 F.Supp. 266, 196 USPQ 544 (D. Conn. 1977), rev'd, 586 F.2d 917, 199 USPQ 641 (2d Cir. 1978), cert. denied, 440 U.S. 961, 201 USPQ 960 (1979). In the first district court decision on Litton's motion for summary judgment, claims 7 and 8 were held invalid for "overclaiming", that is, for claiming an entire ball valve rather than simply an improved sealing ring in the valve. On appeal to the Second Circuit, the "overclaiming" defense was rejected and the case remanded for trial. The technical subject matter of the claims on appeal has been adequately described in these opinions, and familiarity with the discussion contained therein will be presumed. This opinion contains only such background as is necessary for an understanding of the position of the parties on appeal.

[2] Jury interrogatory No. 1 reads as follows:

> 1. Does the ball valve construction shown and described in the Saunders British patent or any other prior art differ in any significant particulars from the ball valve defined by the express language of claims 7 and 8 of the Freeman patent?
>
> As to claim 7 Yes ___ No X
>
> As to claim 8 Yes ___ No X
>
> ° ° °
>
> If you answer "No" as to both claim 7 and claim 8, do not answer any further questions.
>
> The remaining questions were directed to infringement, laches, estoppel and damages. In accordance with the above direction, the jury answered only interrogatory No. 1.

[3] 35 U.S.C. §102(a) reads:

> A person shall be entitled to a patent unless—
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent. ° ° °

Litton responds that elsewhere in the instructions, the jury was instructed on the "clear and convincing" standard of proof.

The record shows that the jury was charged at the close of one day's proceedings. Prior to beginning its deliberations the next day, after discussions with counsel, the court reinstructed the jury that the defendant had the burden of proving by clear and convincing evidence that the Patent and Trademark Office (PTO) was wrong in issuing the patent. The court then went on to instruct that where certain prior art was not considered by the PTO, or if the PTO was misled with respect to what a reference meant, then the burden was merely a preponderance of the evidence. Further, the court advised that, if the patentee were guilty of fraud (despite the absence of a fraud defense in this case), the plaintiff would have to prove that its patent was valid.[4] Finally, the court summed up as follows:

> There's a presumption it [patent] was valid. Can be overcome by clear and convincing proof if certain prior art was not considered. It can be overcome merely by a preponderance of the evidence if the patent examiner was misled as to the meaning of that prior art.

If we assume the transcription is correct, this additional instruction is at best confusing and continues to erroneously vary the quantum of proof depending on the circumstances in contravention of the precedent of this court. Contrary to Litton's argument, an instruction that is defective because of a misstatement of law is not cured simply by a correct statement appearing elsewhere. More is required of jury instructions than to state the law correctly somewhere in the instructions. The question, once a misstatement has been made, is whether the error was so egregious, considering the instructions as a whole, as to require the verdict to be set aside. In this case we hold that it was.

C.

[2] Jamesbury's objections (also made to the district court) that the instructions and interrogatory No. 1, reproduced at note 2, supra, misstate the law respecting novelty were legitimate. The instruction (quoted in B above) to the effect that the claims are invalid if the prior art Saunders patent discloses "substantially the same things" as claims 7 and 8, and Interrogatory No. 1 which speaks of the claims not differing in "significant particulars", are not legally correct.

The error in this interpretation of the statutory requirement of novelty is the same as that which was addressed in Connell, 722 F.2d at 1548, 220 USPQ at 198:

> The opinion says anticipation may be shown by less than "complete anticipation" if one of ordinary skill may in reliance on the prior art "complete the work required for the invention," and that "it is sufficient for an anticipation "if the general aspects are the same and the differences in minor matters is only such as would suggest itself to one of ordinary skill in the art." " Those statements relate to obviousness, not anticipation. Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim. Soundscriber Corp. v. U.S., 360 F.2d 954, 960, 148 USPQ 298, 301 (Ct. Cl. 1966). A prior art disclosure that "almost" meets that standard may render the claim invalid under §103; it does not "anticipate."

Here, as well, anticipation is not shown by a prior art disclosure which is only "substantially the same" as the claimed invention.

Litton argues that elsewhere the district court amplified its interpretation by speaking of the prior art disclosing the claimed invention "in complete terms." However, that additional paragraph of instructions also speaks of "*substantially* the same subject matter * * * *in complete terms, thus enabling* a man skilled in the art to understand and practice the invention." We see no correction of the legal standard in the above statement.

III.

Because of the above legal errors, the verdict of invalidity for lack of novelty (i.e., anticipation) cannot stand. Jamesbury would be entitled to a new trial as a result of those legal errors; Jamesbury moved, however, for judgment NOV. We will, accordingly, turn to the question of whether Jamesbury was entitled to judgment NOV considering the evidence under the proper legal standard of 35 U.S.C. §102. As stated in Connell, 722 F.2d at 1546, 220 USPQ at 197:

> The court must inquire, under the proper legal standard of patentability, whether the evidence and inferences reasonably drawn therefrom, when viewed in the light most favorable to the non-moving party and without weighing credibility, is or is not substantial. [Citation omitted.]

Accordingly, we must determine whether there exists evidence of record upon which a jury might properly have returned a verdict in Litton's favor when the correct legal standard is applied. If there is not, Jamesbury was entitled to have the question removed from the jury and decided as a matter of law. 9 Wright & Miller, Federal Practice & Procedure: Civil §2524 (1972). The standard of review by a court of appeals is the same. The question of whether the evidence is sufficient to create an issue of fact for the jury is itself a question of law, which we will now decide. Id.

The precise question here is whether reasonable persons could conclude that Litton proved by clear and convincing evidence that each and every limitation of claim 7 and 8 is disclosed by Saunders.

The claims in suit are the following:

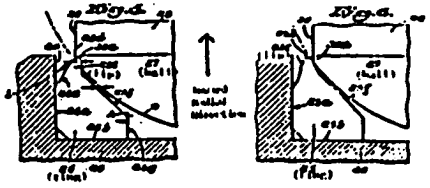
> 7. A ball valve comprising: a casing adapted to be connected to a pipe line and having a valve chamber and inlet and outlet openings; a ball mounted in said chamber and having a port; and a sealing ring mounted in said chamber around one of said openings, *said ring having a lip projecting inward toward the axis of the ring and engaging the ball, said lip being free to bend in the axial direction of the ring and increasing in thickness outward in the radial direction of the ring*, and said ball being rotatable between an open position in which said port is in register with the opening surrounded by said ring and a closed position. [Emphasis added.]
>
> 8. A ball valve as described in claim 7, said lip having side faces disposed one toward the ball and one away from the ball, and said faces diverging from each other substantially uniformly outward in the radial direction of the ring.

Litton does not dispute that the claim language "a lip * * * engaging the ball" means, in light of the specification, that the lip is "pushing against the ball." In the words of the Second Circuit in the previous appeal of this case:

> The seal, which is given a more technical description in claims 7 and 8, has a lip which remains in constant contact with the ball, which may flex to permit rotation and reduce wear, but which is so constructed and placed that it remains tight against the surface of the ball at all times.

199 USPQ at 643.

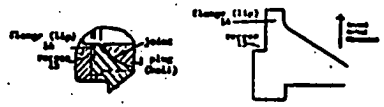
Freeman accomplishes this constant tight contact by a lip on the seal or ring which interferes with the placement of the ball. The lip protrudes into the area where the ball will be placed and is, thus, deflected after the ball is assembled into the valve. Thus:



Because of this constant pressure, the Freeman valve is described as providing a particularly good seal when regulating a low pressure stream.

Nothing in Saunders discloses the lip in one position before assembly with the ball and in a deflected position after the ball is in position. Specifically, Saunders teaches "a narrow flange-like portion to the back of which the fluid pressure has access so pressing this portion against the plug [ball]" and that the ring (but not specifically the lip or flange) is "in engagement with the spherical plug [ball] surface."

The disclosed structure in Saunders is different from that in Jamesbury. As shown in the patent and as more clearly represented by Litton, Saunders shows:



The Saunders specification further states, "It will be observed that the fluid pressure [from left to right] will act mainly on the inner flange-like portion of the ring [14] which is relatively flexible and will therefore be pressed *by the fluid pressure* into good contact with the valve plug [1]." (Emphasis added.) Saunders speaks of improving the seal as the pressure increases.

Nevertheless, relying on the testimony of its expert witness, Professor Youngdahl, Litton maintains that Saunders meets the claim limitation as interpreted to mean constant contact of the lip in a sealing engagement with the ball. His testimony is as follows:

> If that ball were removed, if a Saunders type seal were put in the position so that

[4] In connection with the inequitable conduct defense, we observe that even though expressly withdrawn, the operation of that defense was described to the jury. Under these circumstances, reference in the instructions to a patent owner misleading the examiner was prejudicial. Further, expanding the jury's general knowledge of legal matters not material to the trial does nothing to enhance the jury's comprehension or the proper administration of justice.

the, it engaged the body and then the end cap were bolted up, the Saunders lip would bend away from the end cap increasing the gap that's there and move toward where the ball would be. Of course, when you put the ball in and bolt it up with the ball, you're going to push that lip back. But bending it forward means that it springs that way. Then when you put the ball in and bend it back you have a preloading of the lip and the ball (indicating).

Dr. Youngdahl also testified that he made a model which disclosed this phenomena. Jamesbury's witness disputed the accuracy of the model as a representation of Saunders.

Jamesbury's witnesses testified that the disclosure of Saunders shows no preload or interference between the Saunders flange or lip and the ball, the lip merely touching the ball; that the seal or joint occurs below the lip in the main body of the ring; that under pressure the lip pushes the ball to make a better seal in the main body (compression seating area); and that the lip only sealingly engages the ball when under pressure.

Saunders was considered by the PTO during examination and by the U.S. Court of Claims in an infringement suit on the same claims 7 and 8 against the government. Jamesbury Corp. v. United States, 518 F.2d 1384, 187 USPQ 720 (Ct. Cl. 1975). Litton, through its Contromatics division, was one of the government's suppliers of the infringing valve.[3] Both the PTO and the Court of Claims concluded that claims 7 and 8 were patentable over the Saunders reference. The Court of Claims held, specifically, that Freeman claims 7 and 8 were neither anticipated by nor obvious from Saunders. This decision was based on a finding that:

> [T]he term "engaging the ball" recited in claims 7 and 8 means that the lip contacts the ball with sufficient force to provide a fluid tight seal ° ° ° ° The Saunders flange or lip only sealingly engages the ball 1 on the upstream side when the fluid pressure forces the lip against the ball and never sealingly engages the ball on the downstream side because there is no fluid pressure there to force the lip against the ball. The Saunders sealing ring provides a compression type of seal which depends upon the ball pressing into the material of the ring. ° ° ° The seal of Saunders depends primarily on the contact between the ball and the body of the sealing ring, and the flange or lip sealingly contacts the ball on the upstream side when the fluid pressure increases.
>
> 207 Ct. Cl. 516, 551-52.

Dr. Youngdahl's explanation for the allowance of those claims was, "I don't believe that anyone ever explained the action of the Saunders seat to them and that they understood that there was a preload." Further, Litton asserts that Jamesbury misrepresented to the PTO that a patentable difference existed between Freeman and Saunders in "that the upstream sealing ring of Saunders' ball valve would leak, whereas the upstream Jamesbury sealing ring would not leak." The Youngdahl model assertedly showed that there was no leak.

The issue, of course, is not whether Saunders' valve leaks or does not leak, but whether Saunders discloses a lip which sealingly engages the ball, i.e., whether the Saunders lip functions as the claim limitation requires and whether reasonable persons would find the evidence clear and convincing that it does meet the claim. SSIH Equipment S.A. v. U.S. International Trade Commission, 718 F.2d 365, 383, 218 USPQ 678, 693 (Fed. Cir. 1983), (Nies, J., additional views).

Litton argues that the testimony of its expert, Dr. Youngdahl, which was not before the PTO or the Court of Claims, to the effect that this limitation is found in Saunders is substantial evidence of anticipation. Jamesbury argues that the record as a whole including the unchallenged testimony discrediting Dr. Youngdahl's model of Saunders results in no evidence on which a reasonable jury could find anticipation, particularly in view of the consideration of the Court of Claims and the PTO of the same art. While the decisions of the examiner and the Court of Claims are, of course, not binding in this litigation, we conclude that Dr. Youngdahl's testimony with respect to Saunders is not of such character, when viewed with the reference itself and the contrary testimony of the Jamesbury witnesses, as to overcome clearly and convincingly the presumption of validity, 35 U.S.C. § 282. Nor does it persuade us that deference is not due the full and careful analysis by the Court of Claims and its determination that the lip in Saunders does not sealingly engage the ball at all times. The meticulous opinion of then Commissioner Lane[4] indicates full comprehension of how the valves work. Thus, Dr. Youngdahl's testimony is not substantial evidence, in view of the record as a whole, to support a determination of invalidity for lack of novelty.

[3] This suit concerns non-government sales.

[4] The Court of Claims adopted the opinion of then Commissioner Donald E. Lane (reported at 153 USPQ 672 (1967)), who was later (1969-1979) a judge on the U.S. Court of Customs and Patent Appeals, one of our predecessor courts.

Since a reference which does not satisfy one limitation of a claim does not anticipate, we need not address in detail the arguments of Jamesbury concerning other missing elements in Saunders. We observe, however, that at least one additional limitation of claim 7 is not disclosed therein.

In particular, claim 7 requires that the lip be "increasing in thickness outward in the radial direction of the ring." Referring to Figures 5 and 6 of the '666 patent, reproduced supra, the specification defines "lip" as follows:

> The part of the ring [25] which first engages the ball [27] is a free standing interior lip 25c having a rounded inner surface 25d, and an oblique surface 25e. Leading to the lip is an oblique surface 25f on which the ball will eventually be seated when the lip is deflected sufficiently under load.

Thus, when read in light of the specification, the claimed limitation that the lip increase in thickness outward reads upon the embodiment illustrated in Figures 5 and 6. When this definition of "lip" is compared to the Saunders device, the claim limitation is simply not met. Instead of "increasing in thickness outward" as required in the claim, the properly defined lip portion in Saunders does not change in thickness along its radial axis. It is unimportant that Litton has found a way to redefine "lip" in terms which encompass the Saunders device, since we are compelled to seek such guidance from the specification, and not from the accused infringer.

With respect to claim 8, Litton's witness acknowledged that the geometry of the two lips, which is what the claim specifies, is different.

With respect to other validity issues, Litton specifically withdrew its request for an instruction on obviousness of the claims. The following colloquy occurred during the district court's review of Litton's requested instructions.

> The Court: I think Youngdahl, Professor Youngdahl said this isn't any different than Saunders. He didn't say it's something that's obvious and *so I don't know that any obviousness ever came into play in this case.* You're nodding your head.
>
> MR. SMITH [for Litton]: *No, it didn't.*
>
> The Court: Mr. Smith, so —
>
> MR. SMITH: *I agree.*
>
> The Court: If you agree then I guess I won't have any difficulty with — 35 is out, for one reason, and then 35 through 37, they all deal with obviousness. [Emphasis added.]

In this appeal, Litton did not assert that, if the judgment were to be overturned, Litton was entitled to retry obviousness. Under the circumstances, the issues of obviousness of claims 7 and 8 have been waived.

In view of the absence of sufficient evidence to support a holding of invalidity on the grounds of anticipation, and the withdrawal of alternative attacks on the patent, we conclude that the district court erred in failing to grant Jamesbury's motion for JNOV with respect to validity of claims 7 and 8. Accordingly, the court's ruling on the motion must be reversed.

IV.

Because the issues of infringement, laches and estoppel were not resolved at the conclusion of the trial, the case must be remanded for their disposition. The decision of this court in Envirotech Corp. provides guidance on proper instructions if the issue of infringement is again tried to a jury. As stated therein:

> In general, a finding of infringement depends on whether the accused device falls within the scope of the asserted claims as properly interpreted. Kalman v. Kimberly-Clark Corp., 713 F.2d 760, 770, 218 USPQ 781, 788 (Fed. Cir. 1983). The patented invention as indicated by the language of the claims must first be defined (a question of law), and then the trier must judge whether the claims cover the accused device (a question of fact). see Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1569, 219 USPQ 1137, 1140 (Fed. Cir. 1983); SSIH Equipment S.A. v. USITC, 718 F.2d 365, 375, 218 uSPQ 678, 688 (Fed. Cir. 1983). The patent owner must show by a preponderance of the evidence that the accused [device] has infringed his patent. Hughes Aircraft v. United States, 717 F.2d 1351, 1361, 219 USPQ 473, 480 (Fed. Cir. 1983); SSIH, supra; Chisum, Patents, 18.06[1] (1983).

730 F.2d at 758, 221 USPQ at 477.

Further, the instructions should be tailored to the dispute in this case. As stated in Structural Rubber Products Co. v. Park Rubber Co., 749 F.2d 707, 723, 223 USPQ 1264, 1276 (Fed. Cir. 1984):

> We join other courts that have held that the duty of a trial court in any jury trial is to give instructions which are meaningful, not in terms of some abstract case, but which can be understood and given effect by the jury once it resolves the issues of fact which are in dispute. See, e.g., Choy v. Bouchelle, 436 F.2d 319 (3rd Cir. 1970);

Marshall v. Isthmian Lines, Inc., 334 F.2d 131, 138 n.15 (5th Cir. 1964). Thus, the court should instruct the jury on what the claim means in light of this decison and instruct what elements of the claim are disputed to be found in the Litton valves literally or under the doctrine of equivalents.

Conclusion

For the foregoing reasons, the judgment is *reversed* and the case is *remanded* for disposition of all remaining issues other than the validity of claims 7 and 8 of the Freeman ent No. 2,945,666.
Reversed and Remanded.

Court of Appeals, Federal Circuit

New England Butt Co. v. International Trade Commission

No. 83-1402

Decided Mar. 12, 1985

UNFAIR COMPETITION

1. Appearance of goods or labels — Functional or nonfunctional (§68.207)

Importation restrained under Tariff Act (§68.60)

There is no reason to disagree with International Trade Commission finding, based on idence that accused importer's customer's isted that their respective machine parts be interchangeable with those of complainant, that it is competitively necessary for accused to copy design features and overall configuration of complainant's device, and that design therefore is de jure functional and not protectable as common law trademark, element necessary to make out 19 USC 1337 violation.

Appeal from U.S. International Trade Commission.

U.S. International Trade Commission Investigation No. 337-TA-130, on behalf of New England Butt Co., for exclusion of certain braiding machines for infringing U.S. common law trademark, in which Kokubun, Inc., et al. were named as respondents. From determination that there was no violation of Section 337, complainant appeals. Affirmed.

Norman S. Blodgett, Worchester, Mass., for appellant.

Jack M. Simmons, III (Michael H. Stein, General Counsel, and Michael P. Mabile, Assistant General Counsel, on the brief) for U.S. International Trade Commission.

John W. Simpson, and Kelley, Drye & Warren, both of Washington, D.C. (Francic Y. Sogi and Jeffrey S. Cook, on the brief) for Kokobun, Inc.

Before Baldwin and Kashiwa, Circuit Judges, and Nichols, Senior Circuit Judge.

Baldwin, Circuit Judge.

New England Butt Company appeals from the decision and order of the United States International Trade Commission (Commission) in Investigation No. 337-TA-130, Certain Braiding Machines, under 19 U.S.C. 1337 (1982) (originally enacted as Tariff Act of 1930, Ch. 497, §337, 46 Stat. 703) (hereinafter referred to as section 337), which prohibits unfair methods of competition in the importation of articles into the United States. The alleged unfair trade practice at issue is common law trademark infringement. The Commission ruled there was no violation of section 337. We affirm.

I. Background

New England Butt, established in 1842, manufactures and sells textile equipment. Since 1884, it has manufactured and sold a maypole-type (maypole) braiding machine which is used in the textile industry to manufacture braided material. A maypole braider is so named because the path traced by bobbin carriers on the machine simulates that of dancers dancing around a maypole. New England Butt has made no major design change in its maypole braiders during the one hundred years it has manufactured these machines. The superstructure of the New England Butt braiding machine was the subject of a utility patent which expired in 1938.

New England Butt's Number Two braider is at issue in this case. The braider consists of a series of components, twenty-two of which comprise the alleged trademark. During the 1960's and 1970's Atlantic Braiding Machinery (Atlantic) manufactured and sold a braiding machine very similar to New England Butt's Number Two braider. Atlantic's customers requested that the parts for its braiders be interchangeable with the parts for New England Butt's Number Two braider. The Atlantic braider's resulting similarity in appearance to the New England Butt braider arose from the use of a number of similar componento and assemblies, including the

plate configuration, overall head configuration, vertical uprights, vertical drive shaft, crossbars, brackets, worm gear, and change gear assembly. Differences between the two machines included the drive system and shipper handle.

In 1966, Kokubun, Inc., one of the intervenors, began supplying parts to Atlantic for its braider. Originally, Atlantic supplied sample parts and specifications from which Kokubun produced parts. Later, in 1968, Kokubun began supplying Atlantic with the complete "base group" of the braider. The base group comprised the bulk of the Atlantic machine, everything from the top plate to the bottom plate.

Atlantic went out of business and New England Butt purchased Atlantic's assets. Soon thereafter, Kokubun began to import its braiding machines into the United States through a Canadian sales agent. In 1980, Kokubun engaged intervenor George Sabula as its United States sales representative.

Kobubun has been manufacturing maypole braiding machines since 1922 and has approximately fifty patents directed to braiding machine improvements. Kokubun's 2D braiding machine, sold directly to United States customers after Atlantic's demise, has almost exactly the same structural design as the Atlantic braider. Many parts of the Kokubun braider are interchangeable with parts of the New England Butt Number Two braider. The Kokubun machine also has features different from those of the New England Butt braider, including the change gear guard, stop motion device, take-off support arm, take-off rolls, ceramic former, and work gear guard. Moreover, the Kokubun braider is prominently marked with the Kokubun name and the legend "Made in Japan."

New England Butt filed a complaint with the Commission alleging unfair competition, common law trademark infringement, false designation of origin, and passing off in violation of section 337 in the importation and sale of Kokubun's braiding machines. New England Butt alleged the existence of a common law trademark in the overall appearance of its braiding machine. During the prehearing conference, New England Butt waived all its allegations of unfair acts except for common law trademark infringement.

An Administrative Law Judge (ALJ) conducted a hearing and issued an initial determination which concluded, first, that New England Butt had not proved the existence of a common law trademark in the overall appearance of the braiding machine, second, assuming a trademark existed, there was no likelihood of confusion, and third, the acts complained of substantially injured an industry in the United States, but there is no prospective tendency to substantially injure the domestic industry. Because New England Butt prevailed only on the injury issue, the ALJ held the was no violation of section 337 in the importation and sale in the United States of Kokubun's braiding machines.

New England Butt petitioned the Commission for review of the initial determination. The Commission denied the petition and the subsequent petition for reconsideration. The initial determination thus became the determination of the Commission pursuant to 19 U.S.C. §1335 (1982) and 19 C.F.R. §210.53(h) (1984).

II. Issues

On appeal, New England Butt contends that the Commission erred by determining that the appearance of its braiding machine is primarily functional, and that the braider's appearance is neither inherently distinctive nor distinctive for its having acquired secondary meaning. Further, New England Butt argues that the Commission erred by determining that no likelihood of confusion exists between New England Butt's Number Two braider and Kokubun's 2D braider, and that there is no tendency to substantially injure the relevant domestic industry. Finally, assuming arguendo that a trademark does not exist, New England Butt argues that Kokubun's alleged copying violates the "high level of moral conduct" imposed upon importers by section 337.

III. Opinion

Section 337, in relevant part, declares unlawful: "Unfair methods of competition and unfair acts in the importation of articles ° ° °, the effect or tendency of which is to destroy or substantially injure an industry ° ° ° in the United States." Thus, to prove a violation of section 337, the complainant must show both an unfair act and a resulting detrimental effect or tendency. The standard of review for the Commission's factual findings is the substantial evidence test. SSIH Equipment, S.A. v. USITC, 718 F.2d 365, 371, 218 USPQ 678, 684 (Fed. Cir. 1983).

In reviewing the Commission's determination that there is no section 337 violation, our analysis first turns to whether the overall appearance of New England Butt's Number Two braider functions as a trademark, for without the existence of a trademark, there can be no unfair method or act that can lead to a violation of section 337.

Exhibit C

Decisions of the United States Courts and of the United States Patent and Trademark Office in Patent, Trademark, and Copyright Cases

Court of Appeals, Federal Circuit

In re Sernaker

No. 82-579

Decided Feb. 28, 1983

PATENTS

1. Claims — Dependent (§20.35)

Dependent claims, patentability of which were not argued separately, stand or fall with independent claims.

2. Patentability — Anticipation — Combining references (§51.905)

Assuming that all prior art references are sufficiently related to one another and to related and common art that hypothetical person skilled in art must be presumed to be familiar with all of them, next questions as to whether Board of Appeals correctly deduced obviousness from prior art are whether combination of teachings of all or any of references would have suggested, expressly or by implication, possibility of achieving further improvement by combining such teachings along line of invention in suit, and whether claimed invention achieved more than combination that any or all of prior art references suggested, expressly or by reasonable implication.

3. Court of Appeals for the Federal Circuit — Pleading and practice (§26.57)

CCPA cases reviewing decisions of Board of Appeals under Section 103 are binding precedents in CAFC, as much as CAFC's cases will be; none can be treated as discredited merely because expressions in them can be taken out of their context and construed as in conflict with expressions in other cases.

4. Patentability — Anticipation — Modifying references (§51.217)

Patentability — Evidence of — Suggestions of prior art (§51.469)

It is not necessary that prior art suggest expressly or in so many words changes or possible improvements inventor made; it is only necessary that he apply knowledge clearly present in prior art.

5. Patentability — Anticipation — Combining references (§51.905)

Lesson of In re Imperator, 179 USPQ 730, is that prior art references in combination do not make invention obvious unless something in prior art references would suggest advan-

tage to be derived from combining their teachings.

6. Patentability — Evidence of — In general (§51.451)

Secondary considerations that Supreme Court stated might be of possible utility in obviousness determination, Graham v. John Deere Co., 148 USPQ 466-7, require nonobviousness finding if matter is otherwise doubtful.

7. Board of Appeals — Issues determined (§19.30)

Patentability — Evidence of — In general (§51.451)

Board of Appeals must always consider, in connection with obviousness determination, evidence relating to secondary considerations that applicant properly presented.

8. Patentability — Evidence of — Commercial success — Causes (§51.4555)

Fact that prior art references relied on had not been available to inventor very long and things were moving fast in that industry might justify thought that want filled by invention had not been felt very long, but it does not wholly justify ignoring secondary considerations that speak with unusual eloquence.

9. Affidavits — Distinguishing from references (§12.7)

Patent Rule 116(b) allows examiner to admit affidavit that attests to uniqueness of invention after his final action upon showing of good cause.

10. Affidavits — In general (§12.1)

Board of Appeals — Procedure and practice (§19.45)

Pleading and practice in Patent Office — Rules effect (§54.9)

Under Patent Rule 195, Board of Appeals has power to admit affidavit attesting that invention has met with great commercial success, helped revitalize depressed industry, and introduced new item into marketplace not previously presented upon showing of good cause.

11. Patentability — Evidence of — Commercial success — In general (§51.4551)

Notion that Board of Appeals' bare compliment of appellants' device as "extremely attractive" implies assignment of weight to appellant's commercial success evidence is rejected, since to accept this notion would shrink meaning of phrase "secondary considerations" beyond belief.

Particular patents — Emblem

Sernaker, Embroidered Transfer and Method of Making, rejection of claims reversed.

Appeal from Patent and Trademark Office Board of Appeals.

Application for patent of Howard Sernaker, Serial No. 916,018, filed June 15, 1978. From decision rejecting claims 1-6 and 8-11, applicant appeals. Reversed; Davis, Circuit Judge, concurring in part and concurring in the result, with opinion.

Michael F. Petock, Philadelphia, Pa., for appellant.

Fred W. Sherling (Joseph F. Nakamura, on the brief) for Patent and Trademark Office.

Before Davis, Circuit Judge, Cowen, Senior Circuit Judge, and Nichols, Circuit Judge.

Nichols, Circuit Judge.

This case is before us on appeal from the decision of the Patent and Trademark Office Board of Appeals (board). In a 2-1 decision, the board affirmed the examiner's rejection, under 35 U.S.C. § 103, of claims 1-6 and 8-11 in appellant's application serial No. 916,018, filed June 15, 1978, entitled "Embroidered Transfer and Method of Marking." These claims comprise all the claims in the case. We *reverse*.

I.

Background

A. *The Invention*

Appellant has invented a type of embroidered emblem and a method of making the same. Claims 1 and 10, the only independent claims in appellant's application, are representative of the method and of the emblem, respectively:

1. A method of making an embroidered transfer or emblem comprising the steps of:

(a) embroidering a pattern on a portion of a substrate while using thread free from oil and with said thread being of a single color and in an amount so that a portion of the pattern is sculptured by having a greater thickness that another portion of the pattern,

(b) separating the pattern and its associated substrate portion from the remainder of the substrate,

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ttern is sculptured by having a great-
ickness that another portion of the
n,
separating the pattern and its associ-
ubstrate portion from the remainder
substrate,

(c) providing a transfer print on paper with a dyestuff of at least two different colors and capable of subliming under heat and pressure or vacuum,

(d) registering portions of the print with mating portion of said pattern,

(e) transferring color from said print as a gas to the warp side of the pattern while applying sufficient heat to sublime said dyestuff.

10. An embroidered transfer emblem comprising an embroidered pattern on one side of a substrate whose size corresponds to the size of the pattern with thread of a single color which is free of needle oil, portions of the pattern having a sculptured effect by an increased number of thread stitches, at least two colors of dyestuff printed on the thread stitches defining said portions and on other portions of the pattern, said colors being in registry with said sculptured portions of said pattern with at least one of said printed portions including printing outlining a configuration on a portion of said pattern, and said colors being printed on the warp side of said pattern.

[1] The remaining claims are either dependent on method claim 1 (claim 2–6) or on article claim 10 (claims 8, 9 and 11). For example, claim 2 defines a method in accordance with claim 1 of "applying a thermoplastic adhesive to the shuttle side of the thusly printed pattern." Since neither of the parties argues separately the patentability of each of the rejected claims, the dependent claims will stand or fall with independent claims 1 and 10. In re Burckel, 592 F.2d 1175, 1178–79, 201 USPQ 67, 70 (CCPA 1979).

The claim language includes several key phrases that we should define at the outset. When the inventor uses "registering" and "in registry," he appears by the context to mean placing or placed in correspondence. A "substrate" literally means a basis on which an organism lives, as a plant on the soil. Another common definition of the term in scientific circles is any solid surface on which a coating or layer of different material is deposited. Under both definitions, application to an embroidery is an understandable analogy.

The record includes samples of the "emblems" made by the claimed method, as completed, and in intermediate stages. As completed, the "emblems" are justly characterized by the board as "extremely attractive." They are apparently badges affixed to garments to convey messages about the loyalties, affiliations, tastes, and preferences of the wearer. Would that we judges had something of the sort to brighten up our robes!

The emblem produced by appellant's method resembles an emblem initially embroidered with different colored threads. Appellant's method, however, circumvents the need to embroider the desired pattern with these different colored threads. Rather, a manufacturer following appellant's method first embroiders the pattern with thread of one color on a substrate, separates the embroidery and its associated substrate from the rest of the substrate, and then essentially dyes the threads different colors by use of a transfer print. Such a transfer print consists of two or more dyestuffs on a piece of paper arranged in a pattern mirroring in shape or "mating" the pattern of the embroidery. By placing the transfer print over the embroidery so that the dyestuffs face the embroidery and match its pattern, and then by applying heat and pressure or vacuum conditions, the dyestuffs on the paper will sublime and then adhere to the matching portion of the embroidery.

Before appellant's invention, a manufacturer would use the Shiffli embroidery machine alone to mass produce embroidery. This large machine, however, cannot stitch thread of more than one color at a time. Thus, to create multicolored patterns, the machine would be shut down after each separate color had been embroidered so its 684 needles could be rethreaded with the next color thread. Since each rethreading procedure takes about 45 minutes, the number of different colors that were commercially feasible to use in a single emblem was limited. With appellant's invented method, on the other hand, a manufacturer can produce an emblem of many colors because he needs not rethread the machine anew for each desired color. Instead, only one color (usually white) is used for the entire embroidered pattern, and then the pattern is dyed different colors with one multicolored transfer print.

B. *The References*

The references relied upon by the board are:

Haigh	3,657,060	April 18, 1972
Cox	3,974,010	August 10, 1976
Sernaker	4,092,451	May 30, 1978
British patent	1,243,223	August 18, 1971

Miles, L.W.C., Journal of the Society of Dyers and Colorists, May 1977, pages 161-163.

Vellins, British Knitting Industry, Vol. 46, No. 524, January 1973, pages 45, 46, 48, 50, 53, 55, 57, 59, 63, 65, 67, and 69.

The Butterick Fabric Handbook, Published by Butterick Publishing, A Division

of American Can Company, New York, New York, 1975, pages 99, 100, 119-121, and 142.

The British patent discloses a process of transfer printing on all types of textile articles regardless of their fibers, and a like process of printing on a variety of non-textile articles. With respect to transfer printing on textile articles, the British patent recites a general line of materials to which the process may be applied:

> * * * [F]leeces or webs of non-woven fibers, textile threads, woven webs, knitted material, lace, spongy material in sheet form or already shaped, or even made up articles of clothing.

[British, page 1, lines 68-72.]

The British patent does not specifically mention embroidery as an article susceptible to transfer printing. This patent does, however, teach that a multicolored design may be transferred to textile articles, generally, from a transfer print:

> * * * [S]everal dyes of different colours can be applied on the same support [of the transfer print], these dyes being either intimately mixed *or distributed in order to form the designs* which are to be transferred to the textile articles.

[British, page 2, lines 44-48, emphasis supplied.]

The Miles reference teaches that transfer printing can be done on a variety of substrates, such as susbstrates of polyester and of carpet tile. Miles specifically states that when transferring designs from a paper transfer print to fiber, perfect contact is not necessary because of the vapor state of the dye when it transfers. Although Miles exhibits an awareness of embroidery procedures, he does so in the context of describing the transfer of embroidered patterns onto nonembroidered surfaces; Miles does not teach transfer printing on embroidery itself. Vellins not only teaches transfer printing on a variety of textile substrates (including carpet), but also teaches the deleterious effects of transfer printing on a polyester substrate that contains lubricating oil and other such substances.

The remainder of the references concern various embroidery techniques and methods of producing embroidered emblems, rather than teachings about transfer printing. Butterick reveals that white-on-white embroidery, such as embroidery decoration on a white tablecloth, is commonly made. Butterick also teaches that designs formed in lace can be outlined with embroidery stitching; Butterick defines this entire piece of lace as "re-embroidered lace."

The Haigh patent discloses an embroidered emblem comprised of an embroidered design stitched onto a woven fabric backing material with an embroidered border, and a thermoplastic adhesive bonded to the other side of the backing material.

The Cox patent discloses a method of preparing articles of "aetzed" embroidery whereby a design is embroidered directly onto a backing of thermoplastic material, the design and backing are ironed onto a transfer strip, and then the transfer strip is removed taking with it all parts of the backing not in contact with the embroidery. Embroidery is "aetzed" when heat is used to remove the portions of a backing not in contact with embroidery stitches, so that the embroidered design is left hanging together like lace. The portions of the thermoplastic backing that remain in contact with the embroidery become absorbed or melted into the embroidery as a result of the ironing and serve to improve the bonding of the embroidery stitches and to give the embroidery more body. This improved bonding eliminates the need for underlay and interlock stitches, which would otherwise provide such additional bonding.

The Sernaker patent, issued to appellant in this case, discloses an embroidered transfer wherein a pattern is embroidered onto one side of a diaphanous material with the Schiffli machine, and a layer of adhesive is applied to the other side of this material. When this transfer is ironed onto a base fabric, the diaphanous material melts into the fabric and disappears from view; the transfer thus assumes the appearance of a pattern that is directly embroidered onto the base fabric.

C. *The Rejection*

The board affirmed the examiner's rejection of claims 1, 4-6, and 9-11 [1] under 35 U.S.C. § 103 as obvious in view of British taken with Miles, Vellins, and Butterick. The board also affirmed the rejection of claims 2, 3, and 8 for the same reasons and further in view of Cox or Haigh and Sernaker. The board took the position that appellant's invention in essence consisted of two known elements or procedures: (1) the transfer printing of multi-colored designs from a paper strip onto various types of substrates, including

[1] In Part II, 4 of the examiner's final rejection dated December 3, 1979, the examiner rejected appellant's claims 1-6, and 8-11. In the portion of this letter articulating the reasons for the rejection (Pt. II, 12), however, the examiner inadvertently omitted claim 11 from his discussion of the group of claims to which it belonged. The omission was a typographical error. The board corrected this error when it discussed the examiner's rejection of claims 1, 4-6, and 9-11.

ed onto a woven fabric backing material an embroidered border, and a thermo- ic adhesive bonded to the other side of acking material.

he Cox patent discloses a method of pre- g articles of "aetzed" embroidery where- design is embroidered directly onto a ing of thermoplastic material, the design backing are ironed onto a transfer strip, then the transfer strip is removed taking it all parts of the backing not in contact the embroidery. Embroidery is "aetzed" heat is used to remove the portions of a ing not in contact with embroidery stitch- o that the embroidered design is left ing together like lace. The portions of hermoplastic backing that remain in con- with the embroidery become absorbed or d into the embroidery as a result of the ng and serve to improve the bonding of mbroidery stitches and to give the em- lery more body. This improved bonding nates the need for underlay and interlock es, which would otherwise provide such ional bonding.

e Sernaker patent, issued to appellant in ase, discloses an embroidered transfer ein a pattern is embroidered onto one f a diaphanous material with the Schif- achine, and a layer of adhesive is applied e other side of this material. When this fer is ironed onto a base fabric, the anous material melts into the fabric and pears from view; the transfer thus as- s the appearance of a pattern that is ly embroidered onto the base fabric.

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fabrics, and (2) the making of embroidered transfers or emblems by stitching a pattern of different colored threads onto a substrate.

After noting that appellant had admitted that both of these elements were known in the prior art, the board characterized the manner in which appellant combined them to make a novel article in the following way: "A substrate is stitched with a single colored or white thread and then dyed in the form of a design by transfer printing." Transcript at 75. In the subsequent analysis of the cited references, the board treated various aspects of the appellant's claims as either taught by the references concerning transfer printing or those concerning emblem-making. The board thus reduced the appeal to the question "whether it would have been obvious for one skilled in this art, having these references available, to use the dye transfer process for coloring embroidered emblems." Transcript at 75. The board answered affirmatively, stating:

> After reviewing the references, we come to the conclusion that the dye transfer process has been taught to be usable for almost any type of substrate, from relatively smooth fabrics to materials, such as carpets, which are rough in texture and even to aluminum substrates. The formation of embroidered fabrics is known and, as is taught by Butterick, white-on-white embroidery is commonly made. We believe that one skilled in this art would readily understand that the dye transfer process, as described in these references, and which is acknowledged to be old by appellant, may be used to transfer dye in the form of a pattern to any substrate, whether smooth or rough.
>
> While we find the embroidered emblems extremely attractive, we believe that the process would have been obvious in view of the cited art and that only the expected additive results are obtained. Also, we must not lose sight of the fact that the claims are generic in nature and are not limited to the specific exhibits presented in this case. We must compare the claims with the methods and articles described in the references. When we do so, we come to the conclusion that the claimed process and resulting article would have been obvious to one skilled in this art.

[Transcript at 75-76.]

II.

Opinion

A. *Whether the board correctly deduced obviousness from the prior art.*

[2] We may assume, for purposes of this decision, that all the prior art references in this case are sufficiently related to one another and to a related and common art, that the hypothetical person skilled in the art must be presumed to be familiar with all of them. That being so, the next questions are (a) whether a combination of the teachings of all or any of the references would have suggested (expressly or by implication) the possibility of achieving further improvement by combining such teachings along the line of the invention in suit, and (b) whether the claimed invention achieved more than a combination which any or all of the prior art references suggested, expressly or by reasonable implication. These manifestly related tests are indicated as appropriate by the following decisions of the former Court of Customs and Patent Appeals reviewing, as we do here, decisions of the board denying patentability under § 103 on obviousness grounds.

Cases reversing the board and holding the invention patentable —

In re Rinehart, 531 F.2d. 1048, 189 USPQ 143 (CCPA 1976).

In re Imperato, 486 F.2d 585, 179 USPQ 730 (CCPA 1973).

In re Adams, 356 F.2d 998, 148 USPQ 742 (CCPA 1966).

[3] Cases affirming the board and holding the invention unpatentable for obviousness —

In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In re Conrad, 439 F.2d 201, 169 USPQ 170 (CCPA 1971).

In re Sheckler, 438 F.2d 999, 168 USPQ 716 (CCPA 1971).

And there are many others. All these cases are binding precedents in this tribunal, as much as our own will be. South Corp. v. United States, 690 F.2d 1368, 215 USPQ 657 (Fed. Cir. 1982). None can be treated as discredited merely because expressions in them can be taken out of their context and construed as in conflict with expressions in other cases. Some minds will prefer the results of the first trio, others of the second. The tests stated above, (a) and (b), were the tests applied in all six cases.

The board majority misdescribed the invention by confusing the embroidery with the substrate and in supposing the inventor just applied a print to a rough substrate instead of a smooth one. It compared the invention with the prior art on the basis of the elements employed being print and substrate. Actually, by both claim 1 and claim 10, there are three component elements. The embroidery is introduced between the print and the substrate. No print is applied to the substrate. It is all

applied to the embroidery. The pattern, being "sculptured," intercepts the colors in the print according to the designer's intentions. The print and the pattern (embroidery) are made to "register" (claim 1 and 10 both use this word), i.e., conform. They "mate."

Certainly the board pointed to no prior art that separately suggested expressly or by implication a three-element combination made up in this way. British in general teaches transfer prints on the substrate, as do Miles and Vellins. The remainder do not teach at all about transfer printing. When one skilled in the art at the time of the invention is considering all the prior art in combination, we wholly fail to perceive what more he would have found. The most that would have appeared to have been suggested was the use of transfer prints on rough substrates by which, no doubt, a variety of designs might have been achieved. Mating or registering are suggested nowhere in the prior art. Therefore, it does not show how to approach the results this inventor achieved. No prior art suggests expressly or by implication keeping the print off the substrate and providing a "sculptured" embroidery in a pattern to mate and register with the print.

Although British teaches transfer printing on lace, this patent does not envision the use of a pattern inserted between the transfer print and the lace substrate that would "mate" with the transfer print. Of course the lace substrate itself has an inherent pattern, but British makes no mention of it and does not even hint at mating the transfer print with this pattern. Without some express or implied suggestion, we cannot assume that one of ordinary skill in the art would have found it obvious to mate the transfer print with this pattern. More to the point, the inherent pattern in lace cannot be inserted between the lace substrate and the transfer print because the pattern is part and parcel of the substrate. Even though lace can be "re-embroidered," as Butterick teaches, the embroidery on re-embroidered lace does not initiate a pattern, but merely outlines the pattern of the lace itself; the single colored embroidery described in the first steps of appellant's claimed method, on the other hand, exhibits a pattern of its own designed to mate with the transfer print, and keeps the print off the substrate.

The conclusion is the same under test (b) as it is under test (a). Under test (b), the person who considered merely combining the teachings of prior art references would not expect from the references or any implication to be drawn therefrom that the great advance made by appellant's invention could be attained. The board never showed how the teachings of the prior art could be combined to make the invention.

In re Sheckler, supra, may be taken as an example of a case where a combination of the teachings of prior art references suggested the inventor's result. The invention was for a building block for wall construction comprising a sandwich whose exterior portion were slabs of solid concrete and the interior, bonded to the slabs, was rigid light cellular heat insulating organic foam material. One prior art reference disclosed a reinforced concrete beam with an inner core of foamed polymeric material. Another disclosed a building block consisting of two layers of load-bearing glass separated by an interior layer of heat-insulating foamed glass material.

[4] It could not have placed any great strain on the intellect of the court to sustain the board's conclusion of obviousness. The court said, and we agree, it was not necessary that the prior art suggest expressly or in so many words, the "changes or possible improvements" the inventor made. It was only necessary that he apply "*knowledge clearly present in the prior art.*" Sheckler, 438 F.2d at 1001, 168 USPQ at 717. (Emphasis supplied.)

If this last test is not met, the invention claimed would not have been obvious from the references.

[5] In re Imperato, supra, may be taken as an example of a case when combination of the teachings of prior art references did not suggest the inventor's result. The court therefore reversed the board's holding of obviousness. The invention related to an improvement in the process of "beneficiating" low grade ore to prepare it for the blast furnace. Beneficiation requires grinding the ore to a finely divided state in order to facilitate the removal of impurities. Then, however, it must be recombined into lumps for the furnace. The prior art used various carbonates for bonding to which the inventor added free sulphur. Other prior art taught use of free sulphur only for bonding. The board thought it obvious to combine the two. The court, however, noted that combining both carbonates and sulphur achieved an unexpected result. Both prior processes resulted in lump ore having high strength at low temperatures, but not at high temperatures, whereas the combination obtained a lump ore having high strength in both situations, an unexpected and unobvious result. The lesson of this case appears to be that prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings. It does not appear from

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For the foregoing reasons, it is clear that the principal rejection of claims 1, 4–6, and 9–11 cannot be sustained. The four references relied upon by the board for this rejection (British, Miles, Vellins, and Butterick), either separately or in combination, do not suggest that transfer printing techniques should be combined with embroidery techniques in the specific manner claimed in appellant's application. In view of all the art of record, we also hold that the secondary rejection of claims 2, 3, and 8 must be reversed. While Cox, Haigh, and Sernaker disclose various aspects about the making of embroidered emblems, none of them disclose or suggest transfer printing; they do not envision using transfer printing to create the *effect* of embroidery with different colored threads. Rather, they suggest using standard embroidery techniques, such as hand looming or embroidery with the Schiffli machine alone, to create the embroidered pattern. In the absence of any suggestion to use teachings concerning transfer printing in the making of embroidered emblems, we conclude that appellant's claimed invention would not have been obvious to one of ordinary skill in the art from the above seven references at the time of the invention.

B. *Whether the board correctly disregarded the secondary considerations.*

[6,7] Finally, we hold that the "secondary considerations" that the Supreme Court stated might be of possible utility in an obviousness determination, Graham v. John Deere Co., 383 U.S. 1, 17–18, 148 USPQ 459, 466–467 (1966), also require a finding of nonobviousness if the matter be otherwise doubtful. In an appeal of a rejection of a patent application, secondary considerations, such as commercial success, typically do not play a large part in the analysis of obviousness because the inventor usually waits until his patent issues before he swings production into full gear. Thus, a detailed analysis of secondary considerations is more common in cases like John Deere, which involved infringement. If, however, a patent applicant properly presents evidence relating to these secondary considerations, the board must always consider such evidence in connection with the determination of obviousness. In re Fielder and Underwood, 471 F.2d 640, 644, 176 USPQ 300, 303 (CCPA 1973).

[8] Appellant presented a considerable amount of such evidence. Despite the fact that a patent has not yet issued, appellant has been able to license his invention. Appellant's licensees have sold millions of the emblems, and the Gilardone affidavit attests that appellant's invention has met with great commercial success, has helped revitalize a depressed embroidery industry, and has introduced a new kind of emblem into the marketplace. The DeVries affidavit also attests to the uniqueness of appellant's invention. In addition, the record clearly shows that appellant's multicolored, embroidered emblems are considerably cheaper to produce than the prior art embroidered emblems. It is true the prior art references relied on to establish obviousness had not been available to the inventor very long. Things apparently were moving fast in that industry. This might justify the thought that the want filled by the invention had not been felt very long, but it does not justify wholly ignoring these secondary considerations which here speak with unusual eloquence.

[9,10] In the face of all this evidence, the board was silent. Although the two affidavits in the record before us were submitted after the examiner's decision became final, they were submitted before the board reached its decision. While appellant presented the DeVries affidavit to the examiner after his final action, 37 C.F.R. §1.116(b) (1982) would allow the examiner to admit this evidence upon a showing of good cause. Under 37 C.F.R. §1.195 (1982), the board had the power to admit the later Gilardone affidavit upon a similar showing. The record before us, however, is unclear whether the examiner did, in fact, admit the DeVries affidavit, and whether the board admitted the Gilardone affidavit; neither the examiner nor the board mentioned these affidavits. In response to our specific question in oral argument, however, the solicitor admitted that the "commercial success" affidavits were before the board. In addition, the solicitor cited in his brief the telling Gilardone affidavit and assured us that the board did consider evidence of commercial success. He stated:

> The argument (Br–15), that the Board of Appeals failed to consider the evidence of commercial success, is untenable. The Board specifically stated that they found the embroidered emblems "extremely attractive" (R–76). This appears to be a recognition that the emblems would be well-received commercially. Appellant's af-

fidavit (R-64) [the Gilardone affidavit] shows only that the emblems have had good sales. There is no comparison with the sales of other embroidered emblems.

[11] As we stated above, the Gilardone affidavit shows much more than "good sales." In addition, we reject the notion that the board's bare compliment of the emblems as "extremely attractive" implies assignment of weight to appellant's commercial success evidence. To accept this notion would shrink the meaning of the phrase "secondary considerations" beyond belief. The board in fact said nothing about the commercial success of appellant's invention, and nothing about any of the other considerations the Supreme Court deemed relevant. Although the solicitor assures us that the board did consider the evidence before us relating to secondary considerations, we do not agree with his analysis of this evidence, nor do we find any support for this analysis in the board's opinion.

The solicitor in effect has stipulated that the board considered the evidence, which necessarily implies that it allowed the filing of it on a showing of good cause, as to which there is no other evidence in the record. In view of this stipulation, it appears it would be inappropriate to remand the case for the board to consider the same evidence a second time. We can only conclude that for some unexplained and, to us, unfathomable reason, the board found it insufficient to overcome the, to it, plain indications of obviousness.

For the reasons stated in this opinion, the decision of the board is *reversed.*

Reversed.

Davis, Circuit Judge, concurring in part and concurring in the result.

I join in Parts I and II B of Judge Nichols' opinion. As for Part II A, my judicial microscope suggests to me that, if the prior art is considered alone, the case is much closer than his opinion indicates. Differences there are, of course, between appellant's invention and the prior art, but it is not plain to me, from the bare references alone (especially those disclosing or suggesting transfer printing on lace and other rough-textured or somewhat "sculptured" material), that the invention was not obvious from the prior art. I need not, however, decide that unclear question on the references alone. For me the crucial insight is the "secondary consideration" of commercial success which (as Part II B of the main opinion spells out) appellant has fully proved, the Solicitor has not sought to rebut and has admitted was before the Board, and the Board failed properly to consider. Under Graham v. John Deere Co., 383 U.S. 1, 17-18, 148 USPQ 459, 466-467 (1966), that type of success is a relevant factor, and in this close case I think it decisive in showing nonobviousness.

Court of Appeals, Federal Circuit

Richdel, Inc.
v. Sunspool Corporation

No. 83-611

Decided Feb. 17, 1983

PATENTS

1. Court of Appeals for the Federal Circuit — Pleading and practice (§26.57)

CAFC Rule 7(a) provides that, except for individual appearing pro se, each party and amicus curiae must appear through attorney who is authorized to practice before CAFC; nothing in CAFC rules suggests that exception is to be made due to expense corporation will incur through attorney.

Richdel, Inc., appellant, versus Sunspool Corporation, appellee.

On request of appellee's president to represent appellee. Request denied.

Before Friedman, Rich, and Davis, Circuit Judges.

Per curiam.

Order

This is a request by Harry T. Whitehouse, the president of appellee, Sunspool Corporation, to represent his corporation, which is the appellee in this patent case. Mr. Whitehouse apparently is not a lawyer. He seeks to represent his corporation because "[t]he continuing accrual of professional fees * * * has imposed a substantial financial hardship upon the Appellee."

[1] Rule 7(a) of the Rules of this court provides that "[e]xcept for an individual appearing pro se, each party and amicus curiae must appear through an attorney who is